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THROMBOSIS OF THE DURAL VENOUS SINUSES IN INFANCY AND IN CHILDHOOD

R. K. BYERS, M.D.
AND
G. M. HASS, M.D.
BOSTON

This report was based on the study of fifty instances of thrombosis of the intracranial venous sinuses in infancy and in childhood. We have endeavored to correlate the clinical histories, laboratory data and postmortem studies. An attempt has been made to emphasize a large group of cases to which no definite etiology was assigned. The lesions of the brain consequent to thrombosis of the sinuses and their bearing on neurologic disturbances have been discussed.

HISTORICAL DATA

One of the first descriptions of a probable instance of sinus thrombosis was written by Morgagni (1717).[1] The first accurate study of the condition has been attributed to Abercrombie.[2] In the latter part of the nineteenth century French physicians reported many instances. Bouchut[3] observed thirty cases in twenty-three years. He concluded that thrombosis of the dural sinuses was often found in infants who had convulsions for the first time during the course of febrile or other debilitating illnesses, and that thrombi may form even during convalescence. Rilliet and Barthez[4] found that the majority of their cases occurred during the second year of life. They believed that infections of the alimentary tract and lungs were most important predisposing factors, especially if the infants become emaciated. Haushalter, cited by Bertier,[5] collected four instances in three hundred autopsies of infants.

From the Department of Pediatrics of the Harvard Medical School and the Infants' and Children's hospitals of Boston, and from the Department of Pathology of the Harvard Medical School and the Infants' and Children's hospitals of Boston.

1. Morgagni, J. B.: De Sedibus et causis morborum per anatomen indagatis libri, quinque, Venetiis, ex typog. Remondiniana, 1761, lib. 1, epist. 1, p. 14.

2. Abercrombie, John: Recherches sur les maladies de l'encéphale, translated by A. N. Gendrin, Paris, 1832.

3. Bouchut, J. E.: Clinique de l'hôp ital des enfants malades, Paris, J. B. Baillière et fils, 1884, p. 137.

4. Rilliet, F., and Barthez, A. C. E.: Traité clinique et pratique maladies des enfants, ed. 3, Paris, 1884, vol. 1, p. 219.

5. Bertier, J.: Arch. gén. de méd. **198**:313, 1907.

Holt, according to Blackfan,[6] in two hundred cases of acute nutritional diseases did not find any patients with sinus thrombosis.

CLASSIFICATION

The fifty cases in this series have been divided into two groups. Twenty-six were attributed to infection. The remainder were of obscure etiology and have been interpreted as instances of primary thrombosis.

ETIOLOGY

Sex.—There were thirty male and twenty female patients in the entire series. Boys were more numerous in the group of infectious origin. The same number of instances of primary thrombosis occurred in each sex.

Age.—The average age of the patients with primary thrombosis was 9 months. The oldest was 30 months.

In the infectious group, the average age of those with infections of the mastoid or the scalp was 30 months; of those with meningitis, 11 months, and of those with overwhelming sepsis, 7 months. The youngest patient was a 12 day old infant in whom thrombosis followed an infection of the scalp, and the oldest was an 11½ year old child with mastoiditis. If the cases of mastoiditis were excluded, the great majority were less than 1 year of age.

Incidence.—This collected series included the total number of cases of sinus thrombosis observed at autopsy from January, 1926, to January, 1932. With the exception of the year 1928, there has been during this six year period a gradual increase in the number and frequency of cases. In 1926, eighty-two infants and children were examined. Three and six-tenths per cent showed partial or complete thrombosis of the dural sinuses. In 1931, one hundred and sixty-four cases were examined. Nine and one-tenth per cent of these had sinus thrombosis. These figures apply only to examinations in which the head was included.

Seasonal Data.—The distribution of the instances of thrombosis in which sepsis played the important etiologic rôle was rather uniform throughout the year. In contrast, one half of the cases of primary thrombosis occurred in the months of August, September and October, during which time a large number of acute nutritional disturbances were observed in the clinic.

Nutrition.—The nutritional state was an important predisposing factor. Primary thrombi for many years have been called marantic

6. Blackfan, in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 7, p. 411.

thrombi, because of their occurrence in infants with chronic debilitating diseases. In our series, the clinical course of the majority of the patients was characterized by acute dehydration rather than by chronic malnutrition. Vomiting was common, and severe unexplained diarrhea was the outstanding symptom in sixteen of the twenty-four patients in the primary group. In the infectious group dehydration was also a prominent feature in many instances. Only two infants presented the typical clinical appearance of marasmus.

Infections.—The infections that were most important in initiating thrombosis were those which involved either the wall of the sinus or its tributary veins. Meningitis (twelve cases), mastoiditis (five cases) and cellulitis of the scalp (six cases) were foremost. The remaining three patients each had a severe septicemia without any definite evidence of localization. There were no instances of infections of the face, mouth, paranasal sinuses or nasal cavity, although it is well known that infection in these locations sometimes leads to sinus thrombosis.

The bacteriologic findings were of interest. From the spinal fluid of the patients with meningitis the following organisms were obtained: Bacillus influenzae (six), pneumococcus (two), Bacillus coli (one), Bacillus acidi-lactici (one) and Bacillus tuberculosis (one). Infections of the scalp were due to Staphylococcus aureus in four instances and to Streptococcus haemolyticus in two patients. Cultures from the blood of patients with mastoiditis were positive as follows: pneumococcus (two), streptococcus (two) and Staphylococcus aureus (one). In the cases of overwhelming septicemia Streptococcus haemolyticus (one), Bacillus paratyphosus B (one) and Bacillus pyocyaneus (one) were isolated from the blood stream. Twenty-one of the twenty-four infants with primary thrombosis were studied bacteriologically. All cultures taken from the blood stream and from the spinal fluid before and after death showed no growth.

Etiologic Rôle of Therapy.—The increasing frequency of thrombosis in general, both in Europe and in this country, has been attributed to the increased utilization of intravenous therapy. The possible etiologic importance of this type of treatment in our series of patients will be considered in the discussion of the mechanism of thrombosis.

In relation to therapeutic methods another problem has been presented. In this clinic, blood, saline and dextrose often were injected into the veins of the scalp. These veins commonly became thrombosed. The question arose as to whether the thrombi so produced extended by way of the numerous collateral channels into the large venous sinuses. Although an attempt was made to settle the question, this method of extension was not satisfactorily demonstrated.

The disturbances in the cerebral circulation which were caused by the injection of air into the subarachnoid space have not to our knowledge been important in initiating thrombosis.

It was suggested that the subarachnoid injections of human complement and antiserum caused the high incidence of thrombosis in influenza bacillus meningitis. We believe that there is no well founded basis for this assumption.

Ventricular taps or sinus punctures were not definitely established as the cause of thrombosis. Even though a thrombus is found in the longitudinal sinus after a needle puncture, one should not be overanxious to attribute the thrombosis to trauma. For example, in one patient there was difficulty in obtaining blood from the longitudinal sinus. Finally, the physician withdrew a small clot. The infant died a few hours later. A thrombus was found in the longitudinal sinus. It was shown by microscopic study to be several days old.

Circulatory Disturbances.—It is well known that changes in the blood plasma, blood elements, blood flow and the vessel walls play an important rôle in thrombosis. These factors will be considered in the discussion of the mechanism of thrombosis.

Miscellaneous.—Major surgical procedures were followed by thrombosis in three patients of this series. In these instances there were so many complicating factors that the formation of thrombi could not be attributed with certainty either to surgical trauma or to postoperative circulatory changes.

Progressive hydrocephalus of unknown etiology preceded the formation of thrombi in five infants.

Several authors have emphasized the etiologic importance of a high level of blood calcium. In this regard it may be said that in one patient in this series thrombi developed in spite of the low level of 5.1 mg. of calcium per hundred cubic centimeters of blood.

There were no intracranial neoplasms in our series. Doyle [7] reported the cases of five adult patients in whom tumors obstructed the sinuses. In his opinion compression of the sinus without tumor invasion of the sinus wall did not produce thrombosis.

There were no instances of immediate relationship of thrombosis to contagious diseases. Neither familial nor racial factors were of etiologic significance.

ANATOMY

For a proper understanding of the pathologic changes and clinical course of thrombosis of the dural sinuses, a thorough acquaintance with the anatomy of the sinuses themselves and their principal venous connections and anastomoses was necessary.

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7. Doyle, J. B.: Obstruction of the Longitudinal Sinus, Arch. Neurol. & Psychiat. **18**:374 (Sept.) 1927.

The superior sagittal (or longitudinal) sinus occupies the attached or convex margin of the falx cerebri. Commencing at the foramen cecum, through which it receives a vein from the nasal cavity, it runs from before backward, passing beneath the anterior fontanel and the sagittal suture to the internal occipital protuberance, where its main channel deviates to one side or the other, and is continued as the corresponding transverse (or lateral) sinus. It usually sends a branch to the opposite transverse sinus. It is triangular in cross-section and narrow in front, tending to increase in caliber as it passes posteriorly. In infancy the increase in size is rather sudden just behind the posterior angle of the anterior fontanel. Its inner surface presents the openings

Fig. 1.—The falx and tentorium are shown, with thrombi in the superior longitudinal, right lateral, straight and inferior longitudinal sinuses. Continuing forward from the straight sinus is the thrombosed great vein of Galen and its two tributaries, the venae Galeni.

of the superior cerebral veins, more numerous at the back part of the sinus and partially concealed by fibrous bands. Numerous fibrous bands extend across the inferior angle of the sinus, and, lastly, small openings communicate with irregularly shaped venous lacunae in which are developed the arachnoid villi. The lacunae usually occur as three pairs: a small frontal pair, a larger parietal pair, often occupying the space on each side of the middle fifth of the sinus, and a small occipital pair.

The superior sagittal sinus receives the superior cerebral veins. These are often united into four main trunks, a frontal, a precentral, a postcentral and an occipital vein. The anterior veins enter the sinus at nearly right angles, but the larger posterior veins run obliquely forward,

discharging their blood into the sinus in a direction more or less opposed to the flow of blood within it. These veins drain the superior and mesial aspects of the cerebral hemispheres. The precentral and postcentral trunks usually anastomose with the middle cerebral vein and the sylvian vein, respectively, which in turn are tributaries of the cavernous and superior petrosal or transverse sinuses. The capacity of these anastomosing vessels is variable, but the superior sagittal sinus remains as the chief venous channel for the drainage of the superior and mesial portions of the cerebral cortex.

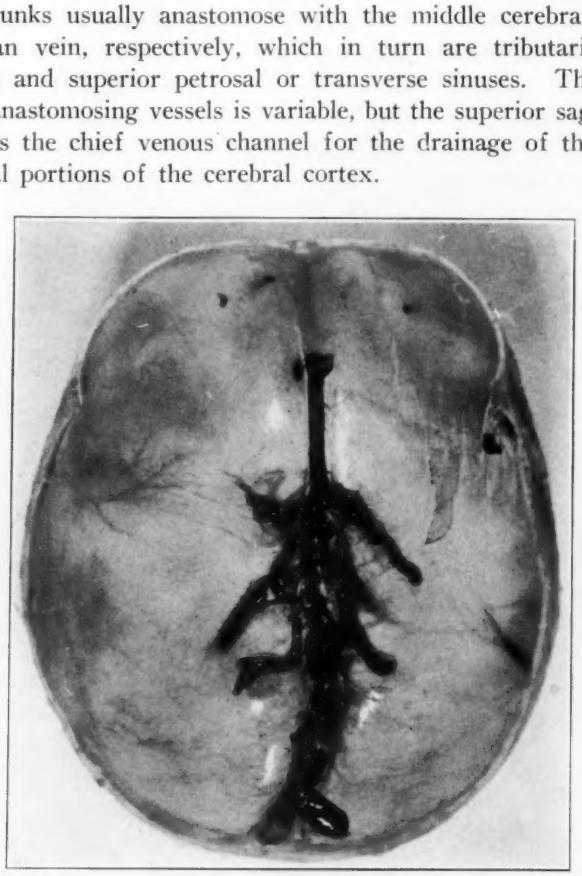

Fig. 2.—The inner surface of the calvarium with a partially organized thrombus in the middle one fifth of the superior longitudinal sinus. Note that the remaining blood clot was of more recent formation. The prominent distended veins leading into the sinus communicated with engorged emissary veins.

Also tributaries of the superior sagittal sinus are veins from the diploe, dura mater and pericranium. The nasal vein entering the sinus by way of the foramen cecum affords anastomoses with the pterygoid and pharyngeal venous plexi. More or less direct communication exists, therefore, between the longitudinal sinus and the veins of the nose, throat, scalp, diploe and brain.

The inferior sagittal sinus occupies the free or concave margin of the falx cerebri, runs from before backward and receives tributaries from the falx and the mesial surfaces of the cerebral cortex.

The straight sinus is situated in the junction of the falx cerebri and the tentorium cerebelli and is a continuation of the inferior sagittal sinus. It receives the superior cerebellar veins and the great vein of Galen, which is the only venous channel of any consequence draining the nuclei in the region of the third and lateral ventricles and much of the white matter of the hemispheres. Although anastomoses between this internal venous circulation and the external circulation carried on through the superior and inferior cerebral veins are said to exist, they are unimportant. The straight sinus runs downward and backward to empty its blood into the transverse sinus of the side opposite that into which the main channel of the superior sagittal sinus is continued. It communicates with the confluence of the sinuses (torcular Herophili) in this region.

The transverse sinuses begin at the internal occipital protuberance and pass laterally and forward in the attached margin of the tentorium to the base of the petrous portion of the temporal bone. Each then leaves the tentorium and passes downward and medialward to reach the jugular foramen. The important tributary veins are the veins of the diploe, the mastoid emissary veins and the condyloid emissary veins by means of which communication is established with the veins of the pericranium. They also receive the superior and inferior petrosal sinuses which anastomose with the cavernous sinuses.

The cavernous sinuses receive tributaries from the veins of each orbit. The orbital veins in turn anastomose with facial veins.

PATHOLOGY

Table 1 describes the position of the thrombi.

TABLE 1.—*Localization of Thrombi*

	Primary (24)	Meningitis (12)	Scalp (6)	Mastoid (5)	Sepsis (3)
Superior longitudinal sinus (entire)	8	8	1	2	2
Superior longitudinal sinus (middle)	10	3	..	..	..
Superior longitudinal sinus (posterior 3/5)	5	..	..	..	..
Superior longitudinal sinus (terminal)	1	1	2	..	..
Cerebral veins	10	8	1	3	3
Lateral sinus (right)	8	6	4	3	3
Lateral sinus (left)	7	4	4	2	2
Lateral sinus (bilateral)	4	3	2	..	2
Straight sinus	6	2	..	1	2
Vein of Galen	3	2	..	..	2

LOCALIZATION

In patients in whom thrombi were of unknown etiology (primary) or secondary to a meningitis, the longitudinal sinus was always partially or completely thrombosed. The thrombi were usually from 3 to 5 cm. in length and were situated in the middle one fifth of the sinus. The clots were firm, friable, grayish red and adherent. The larger thrombi

frequently extended for short distances laterally into the cerebral veins and posteriorly into one or both lateral sinuses and the straight sinus. Although extension posteriorly was most common, the largest thrombi often filled the entire sinus so that in the first and terminal portions, blood clot of more recent formation than that in the middle fifth of the sinus was found.

When thrombi were localized to the lateral sinuses, they were secondary to infections of the mastoids or the scalp. In these instances the thrombi were usually unilateral. In the patients with mastoiditis

Fig. 3.—The superior surface of the cerebrum and the superior longitudinal sinus, which has been opened, are shown. Note the typical localization of the primary thrombus in the middle one fifth of the sinus. The prominent tributary middle superior cerebral veins contain thrombi that are continuous with the thrombus in the sinus.

they originated in the sigmoid flexure of the lateral sinus. From this point they extended not only toward the jugular foramen but also, in two patients, against the flow of the blood, so that the entire length of the longitudinal sinus was filled with blood clot. The thrombi secondary to infections of the scalp usually began near the origin of one of the lateral sinuses and extended for short distances into the opposite lateral sinus and the longitudinal sinus.

Thrombi were rarely found in the large superior cerebral veins except when either the posterior three fifths or all of the longitudinal sinus was occluded by blood clot. In a few instances the small mural thrombi in the middle fifth of the sinus obstructed the orifices of the large superior cerebral veins. As a rule, this obstruction was unilateral, the venous engorgement often being quite prominent. In the more advanced cases the opposite paired veins were also congested. The progression of the thrombus in the longitudinal sinus apparently resulted in thrombosis of these distended cerebral veins, because this usually occurred only in association with a thrombus that occluded either the posterior three fifths or all of the longitudinal sinus.

As is shown in table 2, approximately one half of the patients with primary thrombi had definite cerebral lesions. Similar pathologic changes with variations due to infection were found in ten of the twelve

TABLE 2.—*Pathologic Changes in the Brain*

	Primary (24)	Meningitis (12)	Scalp (6)	Mastoid (5)	Sepsis (3)
Vascular engorgement	12	12	6	4	2
Hemorrhages	12	10	2	3	1
Subarachnoid	12	10	2	3	1
Cortical	10	10	1	2	1
Subcortical	6	5	..	1	1
Necroses	10	10	..	2	1
Cortical	10	10	..	2	1
Subcortical	6	5	..	1	1
Edema	5	12	3	2	1
Hydrocephalus	2	6	..	..	1

patients with meningitis. In only three of the remaining cases were there visible cerebral lesions. Each of those infants had thrombi which filled the superior longitudinal sinus.

In most instances the severity of the pathologic changes in the brain was in direct proportion to the degree and duration of occlusion of the superior longitudinal sinus. The lesions were most common in the meninges and gray matter in the region of the rolandic fissures. Engorged meningeal and cortical veins were prominent. Small cortical and meningeal hemorrhages were often present even though the cerebral veins in several instances contained no thrombi. Large subarachnoid hemorrhages and hemorrhagic foci of necrosis in the cerebrum were almost invariably accompanied by thrombosed veins. Although the multiple small cerebral lesions were usually in the cortex, the larger areas of necrosis often extended into the white matter. The periventricular tissues and choroid plexuses were involved only when thrombi were found in the straight sinus, the great vein of Galen and the venae Galeni. In no instance were there pathologic changes in the brain stem or the cerebellum. Cerebral edema was found only when

there was either extensive sinus thrombosis or inflammation of the meninges. So far as could be determined, hydrocephalus was not a sequel of uncomplicated thrombosis.

MICROSCOPIC APPEARANCE

Microscopic Study of Sinuses.—All thrombi were of antemortem origin. In fourteen of the twenty-four instances of primary thrombosis the wall of the sinus was studied with the thrombus in situ. Even though there was no assurance that the oldest part of each thrombus was selected for histologic study, twelve of the fourteen showed an ingrowth of fibroblasts. In seven instances organization and canalization of the thrombi were moderately advanced. Dense fibrous tissue

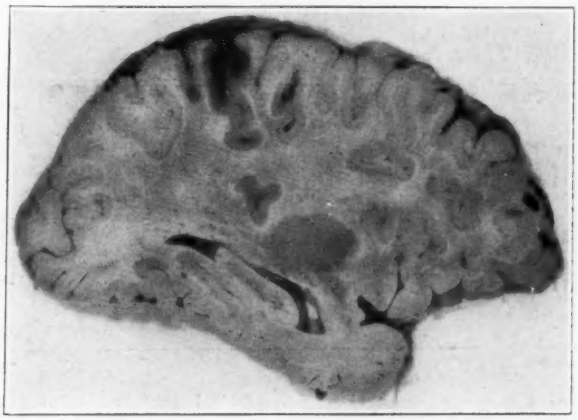

Fig. 4.—This sagittal section of a cerebral hemisphere shows the type of meningeal hemorrhage and cortical necrosis which so frequently follows obstruction of the superior cerebral veins by thrombi.

was found between newly formed capillaries in three thrombi. Polymorphonuclear leukocytes and monocytes were found in the wall of the sinus adjacent to areas of organization in three instances.

In the thrombi secondary to meningitis there was very little organization. A small to large number of polymorphonuclear leukocytes and a few mononuclear cells were invariably found in the sinus wall.

All thrombi secondary to mastoiditis or cellulitis of the scalp showed an ingrowth of fibroblasts. There was canalization in three instances. Acute inflammatory changes were invariably found in the walls of the sinuses.

Only one thrombus in a patient of the group with septicemia was studied. It showed partial organization. There were no inflammatory cells in the wall of the sinus.

Microscopic Study of the Brain.—Microscopic study added little to the information gained from the gross examination. The small hemorrhages in the meninges and cortex usually were found around veins and small capillaries. Hemorrhages were almost invariably associated with the cerebral necrosis. The areas of necrosis often showed evidence of repair. Infiltration of phagocytic cells was common. Rarely, there were formation of capillaries and proliferation of fibroblasts and glia cells. Phagocytes containing hemosiderin were often found in the areas of meningeal hemorrhage. The thrombi in meningeal and cortical veins occasionally were partially organized. In several instances, even though there was no demonstrable infection, inflammatory cells were found in

Fig. 5.—Sagittal section of a cerebral hemisphere, showing unusually extensive lesions. The massive subarachnoid hemorrhage compressed and distorted the configuration of the cerebrum. A large area of hemorrhagic necrosis in the white matter is shown.

the walls and perivascular tissues of thrombosed veins. Welch [8] and Holmes and Sargent [9] made this observation and believe that this cellular reaction may occur in the absence of bacteria.

Pathologic Changes in Other Organs.—The patients who were considered to have primary thrombosis showed little bacteriologic or pathologic evidence of infection. From fourteen of the twenty-four infants in this group blood cultures were taken before and after death. All

8. Welch, in Albutt, T. C., and Rolleston, H. D.: System of Medicine, New York, The Macmillan Company, 1919, vol. 6, p. 691.

9. Holmes, Gordon, and Sargent, Percy: Brit. M. J. **2**:493, 1915.

cultures showed no growth. These were not conclusive data, because it is well known that small numbers of bacteria commonly enter the blood stream and localize in the tissues without producing either a true bacteremia or a septicemia. As a rule, the only pathologic changes were an acute otitis media, a fatty infiltration of the liver and a terminal pneumonia. An acute otitis media was found in eighteen patients. In three of these infants, there was a severe mastoiditis. The incidence of infections of the middle ear and mastoid was only slightly greater in this series than in a similar age group without sinus thrombosis. It seemed improbable that bacteria or their toxins escaping from these foci of infection would so uniformly injure the superior longitudinal sinus. Therefore, they were not believed to be of great direct significance, although they may have been important in initiating the nutritional disturbance.

Thrombi in extracranial blood vessels were uncommon in the group with primary thrombi. They were found in large veins in only two patients. There were no infarcts of the lungs or other internal organs. This was in contrast to the common occurrence of infarction due to embolic fragments set free by purulent disintegration of infected thrombi.

The pathologic changes in the patients with thrombi attributed to infection were variable. However, in each instance there was definite bacteriologic and anatomic evidence of severe infection.

MECHANISM OF THROMBOSIS

Alterations in the blood plasma, the formed elements of the blood, the sinus wall and the blood flow were considered as possible factors that predisposed to thrombus formation.

The majority of the primary thrombi formed during the course of diseases that were characterized by a relatively severe loss of body fluids. The consequent diminution of the volume of blood plasma resulted in an increase in the viscosity of the blood. It was not proved that this change in the physical state of the blood was of fundamental importance, although it may have been a contributory factor.

In six patients in this series the erythrocyte counts were greater than 6,000,000. The number of red blood cells was usually within normal limits. The capillary red blood cell counts, however, were not an accurate indication of the concentration of the formed elements in the large visceral venous channels during the most severe stages of the anhydremia. Overemphasis of the importance of polycythemia was guarded against, because in adults the common conditions which predisposed to sinus thrombosis were chlorosis and chronic debilitating diseases. Chlorosis is characterized by a slight decrease in the number

of red blood cells and a great reduction in the hemoglobin content. It is also true that most patients with chronic wasting diseases have less than the normal number of erythrocytes and lowered hemoglobin values. On the contrary, in adults, thrombosis is common in polycythemia, although thrombi rarely form in the dural sinuses. No blood platelet counts were done. However, the slight elevations in several instances which undoubtedly accompanied the increased concentration of the blood were probably not of great importance. There were no instances of severe anemia.

The use of intravenous therapy paralleled the increasing incidence of thrombosis. Many of the patients in this series were given repeated intravenous injections of saline, dextrose and blood. In other instances intravenous therapy was not used. It is well known that agglutination of the blood platelets is stimulated by intravenous injections of homologous serum, hemoglobin, stroma of erythrocytes and various foreign materials. Also, thrombi form in small capillaries after the injection of bacteria and substances that destroy the cellular elements of the blood. However, with these materials it is experimentally impossible to produce thrombi in large venous channels unless there is a retardation of the flow of blood.

The question arose as to whether or not destruction of the sinus endothelium always preceded thrombosis. There was a definite inflammatory reaction in the sinus wall when the thrombi were secondary to mastoiditis, cellulitis of the scalp and meningitis. This indicated that the endothelium of the sinuses may have been destroyed prior to the formation of thrombi. However, in the patients with primary thrombi and in one infant with severe sepsis, there was no appreciable degree of inflammation in the sinus walls. Although the information gained from the microscopic study was not conclusive, one was inclined to believe that endothelial injury due to bacterial localization was of little importance not only in patients with primary thrombosis but also in several instances in which the thrombi were attributed to infection.

The relation of blood flow to the formation of thrombi was emphasized by Aschoff.[10] Normally the blood platelets circulate in the axial current. They appear in the mural zones when the rapidity of flow is sufficiently diminished (Eberth and Schimmelbusch [11]).

The slowing alone is not sufficient to produce thrombosis because blood in a doubly ligated vessel does not coagulate. However, slowing, eddying and inequality of local conditions facilitate the agglutination of blood platelets. These are then deposited on the endothelium, and

10. Aschoff, Ludwig: Thrombosis, Arch. Int. Med. **12**:503 (Nov.) 1913.

11. Eberth, C. J., and Schimmelbusch, C.: Die Thrombose nach Versuchen und Leichenbefunden, Stuttgart, Ferdinand Enke, 1888.

leukocytes are attracted. The disintegration of the clumps of platelets and leukocytes releases ferments which initiate crystallization of fibrin. Gradually, additional elements are deposited by the flowing stream so that the propagation of the thrombus is usually in the direction of the current. The forming thrombus so changes the flow of blood that fresh nuclei composed of platelets, leukocytes and fibrin repeatedly form.

The influence of the blood flow on the formation of thrombi seemed of etiologic importance in primary thrombosis and possibly in several instances of so-called infectious thrombosis. The midportion of the superior longitudinal sinus was a favorite site for early localization. The rigid sinus wall did not accommodate for variations in the rapidity or volume of blood flow. The sinus had no musculature for propelling the blood. The triangular shape of the channel was such that the surface resistance was greater than that of a circular vessel. There was a sudden widening of the lumen just anterior to the point where the first formed part of many thrombi was located. As this increase in the caliber of the lumen was found just posterior to the anterior fontanel in young infants, it was thought that the depressed fontanel which accompanied dehydration may have accentuated the alteration in blood flow at this point of widening. Furthermore, in this locality there were lacunae, fibrous septums bridging the sinus and numerous cerebral veins which emptied into the sinus in a direction opposed to the flow of the blood. All were possible factors which encouraged the formation and propagation of thrombi.

CLINICAL ASPECTS

Septic Thrombosis.—In this series there were too few patients to allow a satisfactory clinical review. Certain facts, however, are well known. Local infections which have access to the walls of the sinuses either by direct contact or by extension along tributary vessels are most important in the etiology. The first symptom is often a severe headache which is localized in the region of the primary disease. There may be swelling and tenderness over the internal jugular vein. Purulent disintegration of the thrombi gives origin to infected emboli and bacteremia. Positive blood cultures are almost always obtained in these instances. At this stage vomiting, chills and a fluctuating temperature are common. When pulmonary symptoms predominate, septic infarction of the lungs is the most important pathologic change. When abdominal symptoms are severe, the clinical picture may simulate that of typhoid fever. Inflammation of the meninges or brain as a result of extension of the infection is relatively uncommon. In this regard, it may be stated that in the absence of meningitis the onset of stupor, coma or convulsions

early in the course of lateral sinus thrombosis often indicates that there has been retrograde extension of the thrombus into the superior longitudinal sinus.

Primary Thrombosis.—These patients did not present a typical clinical picture. The symptoms were frequently entirely masked by the condition of the infant. When symptoms and physical signs indicated the presence of an intracranial lesion, they differed in the individual cases because they were a reflection of diverse pathologic changes in the brain. These changes usually depended on variable factors such as the extensiveness, duration and rapidity of formation of the thrombi in the longitudinal sinus and cerebral veins.

Therefore, in order to present as clearly as possible this confusing group of patients, a composite study was made so as to emphasize the usual relationship between the symptomatology and the pathologic changes. The patients, as a rule, were between 6 and 18 months of age. A diagnosis of an acute nutritional disturbance was commonly made. Severe persistent diarrhea and vomiting were usually the only symptoms. The physical examination was often negative except for evidence of severe dehydration. The anterior fontanel was depressed, and the respiratory excursions were shallow. The circulation was sluggish. So far as could be determined, it was several days after the onset of persistent diarrhea before a mural thrombus began to form in the longitudinal sinus at a point posterior to the anterior fontanel. If the patient died at this time, there were no symptoms that were suggestive of sinus thrombosis. However, if the thrombus increased in size, the middle superior cerebral veins were obstructed. Consequently, the circulation of the cerebral cortex, particularly that of the motor areas, was compromised. Convulsions were the result. They were usually sudden in onset and jacksonian in type, beginning in an arm or leg and limited to one side of the body. Often they were clonic in nature and, after recurring repeatedly, became generalized. In these patients small hemorrhages were found in the meninges and focal hemorrhagic necroses in the cerebral cortex. In several instances the thrombus was so large that the opposite middle superior cerebral veins also were obstructed. In these patients the meningeal and cortical lesions were bilateral. The increasing obstruction of the sinus was followed by a rapid propagation of the thrombus so that it extended throughout the length of the longitudinal sinus into the medial portions of the lateral sinuses and into the straight sinus. At this stage pain in the head, teeth, face or jaws was a common symptom, and blood was frequently found in the cerebrospinal fluid. During the progression of the thrombus, the condition of the infant became worse. Signs of rapidly increasing intracranial tension developed. Ocular disturbances,

papilledema, stiffness of the neck, bulging fontanel, respiratory irregularities, rigidity and continuous convulsions dominated the clinical picture. At this stage of almost complete thrombosis the intracranial circulation began to rely on collateral channels and in consequence the ocular, scalp, retinal and conjunctival veins became engorged. Edema of the eyelids and of the scalp over the vertex of the skull was sometimes associated with this engorgement. The stupor that characterized these instances of advanced thrombosis was quickly followed by unconsciousness, a sharp rise in temperature and death.

It was often impossible to correlate the clinical and the pathologic findings. The initial convulsions rarely were noted in the first two or three days, more commonly during the second week, and occasionally after several weeks of illness. Furthermore, in several instances there was a period of improvement before the onset of either the first or a second series of convulsions. The recurrence of convulsions usually indicated an extension of the original thrombosis. Most confusing of all were the few instances of extensive thrombosis in which there were neither convulsions nor signs of increased intracranial tension. It was only after superimposing the accumulated data that the foregoing description was completed.

The record of the following patient was selected because it was a typical example of the entire sequence of events.

CASE 1.—A white girl, 1 year of age, had always been healthy until Oct. 16, 1931. She suddenly began to vomit. On the next day the physical examination was negative. Diarrhea developed. Two days later there were convulsive twitchings of her right arm followed by generalized convulsions. She improved and during the next eight days, except for a moderate diarrhea, seemed to be well. On the eleventh day of her illness she was drowsy and irritable. The following day she had rhythmic convulsive movements of the legs and rigidity of the neck, back and extremities. The blood and spinal fluid cultures were negative. The spinal fluid was xanthochromic and under increased pressure. It contained a large trace of globulin, a reduced amount of sugar and 960 cells, 85 per cent of which were polymorphonuclear leukocytes. Generalized convulsions soon developed. Within a few hours engorged right facial veins, edema of the left eyelids and a bulging fontanel became evident. The eyegrounds showed edema of the optic disks and congestion of the retinal veins. Uncontrollable convulsions became almost continuous. The temperature gradually rose to 106 F., and death occurred on the fourteenth day of illness, two days after the onset of severe symptoms referable to an intracranial lesion.

At necropsy, there was seen in the superior longitudinal sinus a thrombus with extensions into many superior cerebral veins, the medial portion of each lateral sinus, the straight sinus, the inferior longitudinal sinus, the great vein of Galen, the venae Galeni, the left superior petrosal sinus, the right cavernous sinus and several veins of the diploe. Microscopic study of the thrombus in the superior longitudinal sinus showed organization by fibroblastic ingrowth and canalization by newly formed capillary spaces. There were cortical and meningeal hemorrhages, and extensive hemorrhagic necroses in the walls of the lateral ventricles.

In contrast to the foregoing patient, the following instance was an example of extensive sinus thrombosis without signs or symptoms of intracranial pathologic changes.

CASE 2.—On March 25, 1929, a girl, 5 months of age, suddenly became ill with an elevated temperature, vomiting and diarrhea. Eight days later, physical examination showed severe dehydration and signs of pneumonia in the lower lobe of the left lung. There were no definite symptoms which indicated cerebral involvement. Because of her stuporous condition, however, a lumbar puncture was done. The spinal fluid, which was under subnormal pressure, showed an increase in globulin, normal sugar, 200 crenated red blood cells and 8 white blood

Fig. 6.—Coronal section of the brain of an infant in whom the thrombi had extended into the venae Galeni. Note the hemorrhagic necrosis of periventricular tissues and of portions of the choroid plexuses. (The brain in case 1.)

cells. Despite the adequate administration of fluids, she failed to improve and died on the twelfth day of the illness.

Postmortem examination disclosed an adherent, firm thrombus which occluded the entire superior longitudinal sinus, four superior cerebral veins, the medial portions of each lateral sinus and the straight sinus. There were meningeal hemorrhages, thrombosed meningeal vessels and small hemorrhagic necroses in the cerebral cortex. A moderate degree of pneumonia and active rickets were the other pathologic findings.

The following case was representative of the usual clinical course and the customary necropsy observations.

CASE 3.—The illness of a boy, 10 months of age, began suddenly with vomiting and diarrhea. He became severely dehydrated. A bilateral otitis media was found. The temperature fluctuated between 100 and 106 F. The ear drums were

incised. He was treated by transfusions and intravenous fluids. On this regimen he improved until the thirteenth day of illness, when he became stuporous and suddenly had twitchings of the right leg and arm and the right side of the face. Three days later there was edema of the eyelids. The convulsions continued and coma supervened. At this time the spinal fluid was under slightly increased pressure and contained 18 white blood cells. The temperature gradually became elevated. He died on the twentieth day of his illness, seven days after the onset of stupor and convulsions.

Postmortem examination disclosed a thrombus originating in the middle one fifth of the superior longitudinal sinus, and extending back to the torcular Herophili. The oldest portion of the thrombus was located at the level of the parietal lacunae. The terminal part of the thrombus was of more recent formation. The large left middle superior cerebral vein contained a thrombus which was continuous with the clot in the sinus. In the drainage area of this vessel there were hemorrhagic necroses of the cerebral cortex and hemorrhages in the leptomeninges. Microscopically, there was partial organization of the anterior portion of the thrombus. In the lungs there was a mild terminal pneumonia. The otitis media was of moderate severity without necrosis of the mastoid bones.

SPINAL FLUID FINDINGS

The spinal fluid was studied in all patients with meningitis, in four instances of mastoiditis and in fifteen infants with primary thrombosis. In the meningeal group, examination of the spinal fluid confirmed the diagnosis of meningitis in each instance. Although repeated studies were usually made, there were no findings that were attributed to a complicating sinus thrombosis. The spinal fluid was abnormal in two patients with lateral sinus thrombosis secondary to a mastoiditis. In one instance there were 13 polymorphonuclear leukocytes and in the other a xanthochromic fluid. In the group of infants with primary thrombi, the spinal fluid was normal in only two of fifteen patients examined. In those two instances the thrombi proved to be mural in type and so small that they did not obstruct the venous channels. In the remaining thirteen infants, the findings were variable. There was an increase in pressure in seven instances. The leukocyte counts ranged from 4 to 960 cells, although values were usually between 10 and 30 cells. The differential counts usually totaled from 30 to 80 per cent polymorphonuclear leukocytes. In seven instances there were from 10 to 300 red blood cells. Grossly, bloody fluid was found twice and xanthochromic fluid three times. Globulin was increased in eleven instances. In two cases there was a diminution of sugar and in one patient an absence of sugar. These three infants had extensive hemorrhagic necroses in the brain and repeatedly negative spinal fluid and blood cultures.

TREATMENT

The early treatment of potential causes of sinus thrombosis should aid in decreasing the incidence. Infections of the air sinuses of the

skull, the middle ears and the mastoids should receive careful attention. Every laceration or infection of the scalp should be regarded as a potential cause of sinus thrombosis. The thrombi secondary to meningitis or to an overwhelming septicemia are of minor importance. The dehydration incidental to vomiting and diarrhea should be treated early and adequately in order to forestall thrombosis as a complication. The indications for surgical intervention in cases of lateral sinus thrombosis are well known and need not be discussed in this report. The surgical

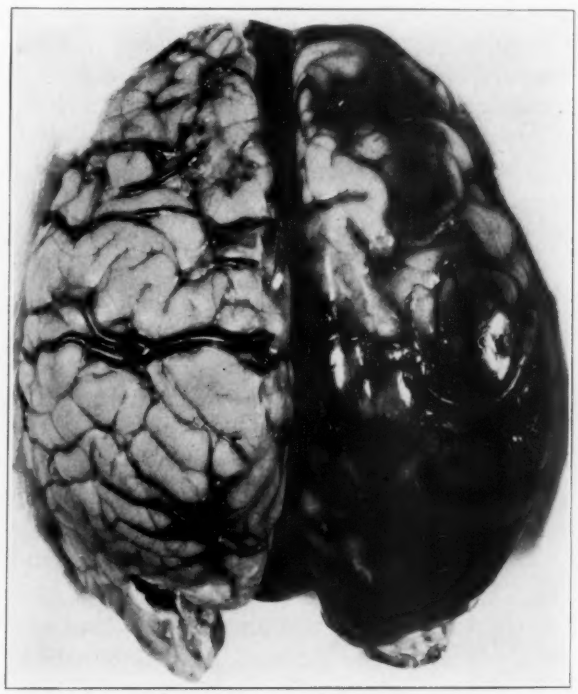

Fig. 7.—Superior surface of the cerebral hemispheres of a patient who had an almost complete sinus thrombosis. The superior longitudinal sinus of this brain is shown in figure 2. Note the cross-striping of the distended thrombosed superior cerebral veins and the unilateral distribution of the massive subarachnoid hemorrhage.

removal of thrombi from the longitudinal sinus may in selected instances prove to be satisfactory therapy. Various methods should be utilized for controlling the increased intracranial pressure with a prospect of success in some patients.

PROGNOSIS

The nature of the primary disease, the location of thrombi, the rapidity of thrombosis, the degree of venous obstruction, the areas of

brain involved by the venous stasis, the efficiency of the collateral circulation and the activity of organization of the thrombus have a bearing on the prognosis. Certain facts which influence the prognosis in infectious thrombosis are well known. The control of the local infection is of great importance. Septicemia and the dissemination of infected emboli are serious complications. Extension of the infection to the meninges or the brain is less common, although when this occurs the prognosis should be guarded. The occlusion of both lateral sinuses does not always indicate an unfavorable termination of the illness. In these instances, adequate control of the increasing intracranial tension may favorably influence the course of the disease. Otherwise, hydrocephalus and a variable degree of cortical damage may occur. When thrombi, which originate in the lateral sinuses, obstruct the superior longitudinal sinus, the immediate prognosis is poor. If these thrombi extend into the straight sinus and its tributaries, a fatal outcome is to be expected. If thrombosis becomes so extensive that edema of the eyelids and scalp develops, there is little chance for recovery.

The prognosis in the instances of primary thrombosis is variable and in many respects is based on theoretical considerations. Mural thrombi, if they do not occlude the longitudinal sinus or cerebral veins, are usually harmless. In some instances small mural thrombi so obstruct cerebral veins that serious cortical lesions are produced. As a rule, the pathologic changes in the brain are neither of sufficient severity nor in the proper location to cause death. The sequelae will depend largely on the areas of cortex involved. As the superior middle cerebral veins are most frequently thrombosed, temporary or permanent dysfunction of the motor cortex may be the most commonly expected complication. The function of other cortical areas also may be disturbed.

It is generally accepted that the appearance of neurologic symptoms due to a lesion of the brain acquired in infancy often coincides with the functional development of the involved part of the brain. For this reason, an apparent complete recovery from the acute lesions of sinus thrombosis does not insure against a subsequent neurologic disturbance.

In the past it has been assumed that sinus thrombosis of sufficient magnitude to cause appreciable pathologic changes in the brain was only a terminal disease of moribund patients. There was little evidence which indicated that infants might survive such an impairment of the cerebral circulation. Ferrari [12] was able to obstruct the intracranial sinuses of dogs without fatal consequences. Doyle [7] reported three cases with occlusion of the longitudinal sinus by meningiomas.

12. Ferrari: Med. Jahrb. d. K. K. gesellsch. der Aerzte **3**:81, 1888.

Hershey [13] recorded one instance in which complete obstruction of the longitudinal sinus followed a fracture of the skull. The patient recovered. In this clinic a boy who had infectious sinus thrombosis with occlusion of both lateral sinuses was treated successfully by ligation of the internal jugular veins and repeated lumbar taps to reduce the increase in the intracranial pressure. Macewen [14] mentioned three patients in whom thrombi were demonstrated in the longitudinal sinus at operation. These patients recovered. Holmes and Sargent [9] observed many adult patients with longitudinal sinus thrombosis of traumatic origin. The patients often improved with surprising rapidity.

The following case history was selected from the records of this clinic because it exemplifies one of the many possible sequelae of sinus thrombosis.

CASE 4.—E. P. was born in September, 1930. She sat up at 4 months, walked at 11 months and began to say a few words at 14 months of age. At 15 months of age she started to vomit after each feeding. Vomiting increased in frequency, and a mild diarrhea developed. One week after the onset of vomiting she was admitted to the hospital. Physical examination, except for pallor and evidence of severe dehydration, was negative. During the next three days, two clyses and two intravenous injections of dextrose solution were given. Vomiting ceased. The following day she had a severe generalized convulsion. This lasted one hour. A lumbar puncture showed a moderate increase in pressure and normal dynamics. Examination of the cerebrospinal fluid showed normal sugar, positive globulin and 1,210 cells, of which 1,168 were red blood cells and 42 were white blood cells. Eighty per cent of the white blood cells were mononuclears. Cultures of the spinal fluid were negative. Blood cultures taken on the day of the first convulsion and on the following day were negative. Convulsions continued. Bilateral spasticity, greater on the left, developed. Repeated lumbar taps for several successive days gave findings similar to those first recorded. However, nine days after her first convulsion the red blood cells disappeared from the spinal fluid. After five more days the cell count and globulin returned to normal. The dynamics remained normal throughout.

As the acute symptoms subsided, she was obviously spastic and idiotic. She was discharged from the hospital. One month later and approximately two months after her first convulsion, an encephalogram showed marked dilatation of the lateral and third ventricles with a large amount of air over the convexity of each cerebral hemisphere. Her hopeless condition for the past six months has remained unchanged.

Exceptions may be taken to the diagnosis in this case. Nevertheless, the most logical assumption was that a thrombus formed in the superior longitudinal sinus and extended into the major cerebral veins. Severe cerebral lesions were the immediate result, with the subsequent development of idiocy, spasticity and cerebral atrophy. In review, we emphasize the age of the infant, the period of normal development and then the

13. Hershey, D. W.: Boston M. & S. J. **61**:336, 1859.

14. Macewen, William: Pyogenic Infective Diseases of the Brain and Spinal Cord, Glasgow, J. Maclehose & Sons, 1893.

acute illness with dehydration, the subsequent sudden repeated convulsions, the bloody spinal fluid, the negative bacteriology and the residual severe cerebral damage.

COMMENT

The fifty instances of sinus thrombosis which have been presented were divided into two groups. A certain number of cases were attributed to infection. No etiology was assigned to the remainder.

Those infants in whom thrombi of the primary type developed had a number of characteristics in common. They were less than 30 months of age. They often suffered from acute nutritional disturbances. Dehydration consequent to vomiting and diarrhea was usually the only important physical finding. The thrombi, almost invariably during the first or second week of the disease, formed in the midportion of the superior longitudinal sinus and propagated so as to produce stasis and coagulation of the blood in the tributary cerebral veins.

It seemed that the most important factors in determining the site of localization in the sinus were the anatomic features that favored slowing and eddying of the blood current and any disease that produced concentration of the blood and sluggish circulation.

The clinical picture of primary thrombosis was quite variable. The condition was rarely diagnosed. Symptoms referable to an intracranial lesion appeared only after the circulatory obstruction had produced pathologic changes in the meninges and the cerebrum. However, the hemorrhages in the meninges and hemorrhagic necroses in the cerebral cortex did not always produce symptoms or suggestive physical findings. The development of convulsions during the course of an illness or even after recovery was of important diagnostic value. Symptoms of meningeal irritation or evidence of hemorrhage into the subarachnoid space were frequently overlooked by the physician. Indeed, several cases were diagnosed as encephalitis.

There was every reason to believe that many patients with primary sinus thrombosis must survive. This study did not permit statements of fact in this regard, but, nevertheless, one might be allowed to predict certain sequelae in event of recovery. In certain cases there would be no residual anatomic change. In others, survival would presumably be followed by organization, resorption and virtual disappearance of the thrombi, with only a small amount of fibrous tissue to mark their former sites. Hemosiderosis, cystic degeneration, gliosis, calcification and atrophy of portions of the brain might well be expected to occur in the weeks and months following the original disease. Canalized thrombi, fibrosis, hemosiderosis, partial obliteration of the subarachnoid space, subarachnoid cysts and groups of newly formed blood vessels might eventually mark the sites of hemorrhages into the leptomeninges.

Hydrocephalus might develop as the result of interference with the absorption of spinal fluid. There are many other possibilities, but as the final pathologic picture is obscure, a sufficient number of assumptions have already been made.

These predictions have been advanced possibly without adequate proof. Nevertheless, if sinus thrombosis as a puzzling and often unsuspected complication of disease is kept constantly in mind, the etiology of certain instances of "encephalitis," spontaneous subarachnoid hemorrhage, cerebral palsy, cortical atrophy, mental defectiveness, epilepsy and hydrocephalus may then become apparent.

ACUTE RHEUMATISM AS A FAMILIAL DISEASE

EDITH IRVINE-JONES, M.B., CH.B.
ST. LOUIS

This study of rheumatism has been pursued for several years and in two large pediatric clinics, that of Washington University, St. Louis, and that of the University of Toronto, Canada. Five hundred families with rheumatic members were investigated; this represented more than eight hundred rheumatic persons in the immediate family circles. This was necessarily largely a study of rheumatism as a familial disease, and it was felt that the value of such observations lay not only in the considerable number of families represented, but in the comparison by one observer of rheumatism in two widely differing communities.

By the methods used it was hoped to show the relative importance of heredity and constitution contrasted with infectivity as factors in the occurrence of rheumatism.

In the two clinics the methods of obtaining data were similar. The mother of every rheumatic child examined was questioned as to the occurrence of rheumatism in other members of the family, and asked to bring in the other children and, when possible, the father for examination. By means of evening clinics and visits to the homes a large percentage of the "contacts" of rheumatic children were questioned and examined. The social conditions of the subjects at the two clinics were regarded as comparable.

The manifestations regarded as rheumatism included acute rheumatic fever, chorea, shifting joint pains without fever, and mitral stenosis. Hospital or clinic records, military hospital records and diagnoses made by outside physicians were accepted in most cases. The statements of parents were also accepted as evidence of rheumatism in relatives who were not available for examination (usually deceased or out of the country), if in such cases a physician had made a diagnosis of "inflammatory rheumatism with a leaking valve" or "St. Vitus' dance."

Cases were omitted in which a systolic apical murmur, apparently organic, was unaccompanied by a history of rheumatism, although it was

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From the Department of Pediatrics, University of Toronto, Canada, and the Department of Pediatrics, Washington University School of Medicine and the St. Louis Children's Hospital, St. Louis.

felt that many such cases may have been rheumatic. It was also felt advisable to omit children under 3 years of age, owing to the rarity of rheumatism in children under that age.

The material used for this study is summarized in table 1.

It will be seen from table 1 that in both communities the proportion of families showing mutiple cases of rheumatism is about one third.

A third series of subjects was obtained as a control group from the three following sources in Toronto: (1) families of children attending the heart clinic for some symptom or cardiac sign other than a rheumatic one; (2) families attending the chest clinic, largely tuberculosis contacts, and (3) families attending the holiday camp at Bolton, Ontario. It was felt that in race and social conditions these families were com-

TABLE 1.—*Summary of Clinical Material Used*

Heart Clinic of the Hospital for Sick Children, Toronto	Families	Rheumatic Persons
Number of families represented in clinic by one case of juvenile rheumatism	333	333
Number of families represented in clinic by multiple cases of rheumatism (including parents as cases)	166	487
Total families	499	820
Percentage of families showing multiple incidence of rheumatism	33	
Children's Heart Clinic of Washington University and the St. Louis Children's Hospital		
Number of families represented in clinic by one case of juvenile rheumatism	113	113
Number of families represented in clinic by multiple cases of rheumatism (including parents as cases)	54	144
Total	167	257
Percentage of families showing multiple incidence of rheumatism	32	

parable with the "rheumatic" group, and a total of seventy such families were studied.

RELATIVE INCIDENCE OF RHEUMATISM IN "RHEUMATIC" AND "NONRHEUMATIC" FAMILIES

For this comparison one deducted from both the Toronto and the St. Louis "rheumatic" families all of the original cases of rheumatism in which the patients were examined at the clinic. When this was done, it was found that the Toronto families still showed an incidence of sixty-four rheumatic persons per hundred families and the St. Louis group, fifty-four per hundred families, while the incidence in the control group (obviously with no deductions) was thirty-one per hundred families. Thus when a member of a family showed clinical rheumatism, the chance of rheumatism appearing in other members of the family was practically doubled.

STUDY OF FAMILIES SHOWING MORE THAN ONE CASE OF RHEUMATISM

The study was henceforth confined to those families in which there was more than one case of rheumatism, and an intensive examination was made of a large proportion of such families. In St. Louis, fifty of the fifty-four families were completely studied and blood groupings were made in addition; in Toronto a hundred of the one hundred and sixty-six families were picked out for a complete study.

In this way it was found that the more complete the examination, the higher the proportion of persons found to be rheumatic. Thus while for the grand total of families with multiple incidence (two hundred and twenty) the family incidence was 2.9 members affected, the incidence for the one hundred and fifty families intensively studied was 3.2 per family. Wide variations were found in the number of persons

TABLE 2.—*Number and Proportion of Offspring Affected in Various Groups of Rheumatic Families*

	Clinic			
	Toronto		St. Louis	
Affected Parent	Number of Families	Proportion of Family Affected, per Cent	Number of Families	Proportion of Family Affected, per Cent
Neither parent affected	17	51	11	48
Father only affected	18	67	13	59
Mother only affected	43	55	25	38
Both parents affected	22	46	1	33

affected in each family; in St. Louis the number varied between two and six, and in Toronto, between two and nine. The actual proportion of the family affected was higher in Toronto, being 52 per cent, while in St. Louis it was 42 per cent.

Whether the heavy incidence of rheumatism in such families was due to contagion or to a hereditary constitutional factor was next investigated.

It was felt that if the disease were hereditary, the number of children affected would depend on whether one, both or neither parent was affected. This has been shown by Cooke and Vander Veer [1] to occur in the inheritance of atopic hypersensitiveness. The families were therefore grouped according to whether: (*a*) neither parent was affected, (*b*) only the father was affected, (*c*) only the mother was rheumatic or (*d*) both parents had had rheumatism. In both the Toronto and the St. Louis clinics, the group in which the mother was the rheumatic parent was the largest. However, it is noteworthy that in the group in which the father was affected, the percentage of rheumatic offsprings was the highest. The percentages are shown in table 2.

1. Cooke, R. A., and Vander Veer, A.: J. Immunol. **1**:215, 1916.

The large number of families in which the mother was affected could be easily explained by the higher incidence of many of the rheumatic manifestations in females. It was more difficult to explain the large proportion of rheumatic children in families in which the father was affected. That closeness of contact was not a factor is obvious, since, if that were a determining factor, a larger proportion of children would be infected when either the mother or both parents were rheumatic.

A further study of these figures was made to see whether there was any peculiar distribution of the children as to sex in the four groups. In his study of the subject, Draper [2] concluded that when the father was rheumatic the percentage of boys affected was lowest, and that when the father was unaffected the percentage of boys affected was highest. Our figures did not support this conclusion. They point, however, to a definite difference in the sex distribution of rheumatism in families in which the father was rheumatic (table 4). For this table

TABLE 3.—*Sex Distribution of Rheumatism in Families*

Affected Parent	Percentage of Boys Affected	Percentage of Girls Affected
Neither parent affected	43	60
Father only affected	45	79
Mother only affected	44	59
Both parents affected	48	54

each family was divided into the proportion of affected boys and of affected girls. The results were added for each group, and percentages were obtained. The figures given thus represented the percentage of rheumatic boys or girls of the total number of boys or girls in the families studied.

From these figures it seems apparent that in our series the proportion of boys affected was constant and low, and that it is irrespective of the amount of parental rheumatism. The proportion of girls affected was always higher, and apparently varied with the parental infection. Thus when both parents were rheumatic, only 54 per cent of the total girls were affected, while when the father alone was rheumatic, the percentage rose to 79 per cent. Since the number of girls in the four groups exceeded the number of boys, there was a much greater amount of rheumatic infection in girls. The figures for Toronto and for St. Louis were similar, and this fact lends significance to them.

It is thought possible that the susceptibility to rheumatism may be transmitted from affected father to daughter. One would then have to postulate some other mechanism to explain the lowered percentage

2. Draper, G.: Am. J. M. Sc. **171**:803, 1926.

when both parents are rheumatic. The figures do not seem to justify one in supposing that the opposite condition exists, namely, that the sons may inherit a mother's susceptibility.

In studies of the inheritance of atopy, it has been shown by Cooke and Vander Veer and by Spain and Cooke [3] that when the atopic characteristics are present in both parents, the children present symptoms of atopy at an earlier age than when the inheritance is unilateral. It was felt that this might hold in rheumatic infections. To study this point, the families were again divided into the four groups and the ages of children at the time of their first attack computed. The average ages in the four groups and in the two communities are given in table 4. It will be seen that the rule of earlier manifestations with a double inheritance does not hold in rheumatism, and that whether the father or the mother is the susceptible subject makes little difference in the age at onset. One significant point arising from this study is that the Toronto subjects were appreciably younger (8.1 years) than

TABLE 4.—*Average Age at Onset of First Rheumatic Manifestations in Various Groups*

Parent Affected	Toronto, Average Age, Years	St. Louis, Average Age, Years
Neither parent affected	7.6	8.7
Father only affected	8.1	9.6
Mother only affected	8.1	8.9
Both parents affected	8.3	1 family only
Average age for all	8.1	9

the St. Louis subjects (9 years) when the first manifestation of rheumatism occurred.

INCIDENCE OF RHEUMATISM IN DISTANT RELATIVES AND UNRELATED CONTACTS

It was felt to be of importance to study the incidence of rheumatism in the relatives of rheumatic subjects outside the immediate family. These relatives were grouped according to whether they resided with the family or distantly. Many relatives of Toronto subjects were still resident in England and Scotland, and when the health of those subjects was definitely known such relatives were included. Persons who lived with rheumatic families but who were unrelated, such as foster children and boarders, were also investigated. The results were compared with those found in the control group.

In the smaller group of persons actually living in close contact with the rheumatic families, it was found that rheumatism occurred in about

3. Cooke and Vander Veer (footnote 1, p. 210). Spain, W. C., and Cooke, R. A.: J. Immunol. **9**:521, 1924.

25 per cent of the unrelated boarders and in 65 per cent of those who were related. Since the total figures involved were less than twenty, they may not be significant. The amount of contact in the two types was approximately the same, as most of the unrelated members were foster children who slept with the members of the family. This might point to the importance of a rheumatic constitution in the production of the disease.

A study of relatives of rheumatic subjects outside the immediate family was more difficult to make. In several of the cases, cousins and youthful aunts and uncles attended the clinic, or had been treated in the hospital for rheumatism, or had presented themselves for examination, but in many instances the relatives were classed as rheumatic, nonrheumatic or dubious according to the descriptions given. It is also possible that when rheumatism existed in a family the parents were more observant of the same symptoms occurring in their relatives, whereas the control group of families was not sufficiently interested to remember such a condition in relatives.

The figures for the two communities of St. Louis and Toronto were found to be in close agreement as to the amount of rheumatism present in relatives. In about one third of the families there were definite instances of rheumatism; in another third, rheumatism was said to be absent; in the remaining third the presence of rheumatism was dubious, or the relatives were scattered and their health not known. On the other hand, rheumatism could be found in the relatives of less than 10 per cent of the families in the control group.

RHEUMATISM IN IDENTICAL TWINS

In the series of one hundred and fifty families with multiple cases of rheumatism, there occurred ten pairs of twins; two pairs were identical; seven pairs were nonidentical, and one pair was doubtful, as one of the children had died in Europe.

Rheumatism was present in both children of each pair of the two pairs of identical twins. In one family, both had simultaneous attacks of rheumatic fever at 8 years of age, and in the other family both children were brought to the clinic together at the age of 6 years with growing pains. One child of the first pair had questionable carditis; the others were free from clinical heart involvement.

Of the nonidentical twins, two pairs were free from rheumatism. In each of the remaining five pairs there was one rheumatic and one healthy child. The difference between the incidence in the identical and the nonidentical twins was striking, even with the small numbers represented, as the contact between nonidentical twins is considerable even when the sex is different.

THE BLOOD GROUPS IN RHEUMATIC FAMILIES

The relationship between the blood groupings and the incidence of disease has been worked out for many supposedly familial diseases. Herzfeld and Brokman [4] have traced the inheritance of sensitivity to diphtheria to factors inherited with the blood group. Levine,[5] with more exactness, attempted to correlate the inheritance of atopic hypersensitiveness with the inherited groups, but was not successful in showing any relationship. Others have used the same procedure for different diseases, with varying results.

For this study we grouped thirty-four of the fifty-four St. Louis families, a total of one hundred and eighty-seven persons, eighty-nine being rheumatic and ninety-eight nonrheumatic. We were anxious to determine: (*a*) whether any particular agglutinogen or combination of agglutinogens was characteristic of the rheumatic subjects; (*b*) whether the child of a rheumatic parent who inherited the group of that parent was necessarily rheumatic; this might throw light on the

TABLE 5.—*Blood Groups of Rheumatic Subjects*

Blood Groups	Rheumatic	Nonrheumatic	Blood Groups	Rheumatic	Nonrheumatic
O.....	30%	26%	B.....	6%	8%
A.....	55%	50%	AB.....	9%	9%

high percentage of girls affected when the fathers were rheumatic, and (*c*) whether heart disease, as distinct from joint and nervous manifestations of rheumatism, might tend to occur particularly in children of any one group.

It was found that when the subjects were divided into two classes, rheumatic and nonrheumatic, similar percentages for the occurrence of different blood groups obtained. Thus no rheumatic-susceptible characteristic was associated with any of the groups.

The cases were again reviewed to see whether more patients who acquired organic heart disease belonged to a certain group; it was found that 51 per cent of those with a cardiac condition belonged to group A and 35 per cent to group O. Thus the greatest difference shown was between the nonrheumatic patients in group O (26 per cent) and those with rheumatic-cardiac conditions in that group (35 per cent). With rather small numbers, particularly in the last series, it is difficult to attach significance to the difference in percentages.

It was felt that children might inherit rheumatism along with the corpuscular elements of the susceptible parent. For this determina-

4. Herzfeld, L., and Brokman, H.: J. Immunol. **9**:571, 1924.
5. Levine, P.: J. Immunol. **11**:283, 1926.

tion many families were excluded, namely, those in which neither parent or both parents were affected, those in which both parents had the same blood group, those in which the rheumatic child belonged to group O, regardless of the groups or infections of the parents, and those in which the susceptible parent and the susceptible children were in group O, as again they did not necessarily inherit the blood group of the susceptible parent. Frequently, in families in which the susceptible parent and some susceptible children were in group O, other susceptible members had agglutinogens, and in such cases only the latter group was considered. It was found that only thirteen families were left that fulfilled the requirements. These were divided into three groups, as shown in table 6.

It will be seen from the table that group C is no larger than group A, and thus that the blood of rheumatic children may or may not be in the same group as that of the affected parent.

TABLE 6.—*Blood Groups in Various Types of Families*

Group	Type of Family	Number of Families
A	Families in which the affected children had a blood group different from that of the affected parent	6
B	Families in which more than one child was affected; one had same group as affected parent; one different	2
C	Families in which the affected child had same group as the affected parent	5

THE COLORING OF RHEUMATIC SUBJECTS

Much has been written regarding the coloring of rheumatic children, and a great deal seems to be contradictory. It was felt that with two separate communities to study, consistent findings as to coloring would be of significance.

Racially the St. Louis group was more mixed than the Canadian group. In St. Louis, practically all the parents of the families were American-born and included English, Irish, German, Slavic, Jewish and Italian people and Negroes, in that order of frequency. On the other hand, in Toronto about half of the children and very few of the parents were Canadian-born. The great majority were settlers from Scotland and England. The other races represented were Irish, Jewish, Slavic, Italian and Finnish. In St. Louis there was a preponderance of blonds (41 per cent), and 8.2 per cent of the subjects had clear red hair. The nonrheumatic relatives included 40 per cent blond and 3.5 per cent red-haired persons. In Toronto, the percentage of blonds was somewhat higher (52 per cent) and the percentage of red-haired persons was 12. The nonrheumatic relatives showed the same proportion of blonds,

but rather fewer with clear red hair. The control group, however, was definitely darker, and although in it were included the rheumatic subjects that occurred, only 34 per cent were classed as blonds and 5.6 per cent as red-haired.

The eyes were also noted as being blue, blue-gray, blue-yellow, green, hazel or brown. In both communities there was a preponderance in the rheumatic group of the mixed type of blue with yellow, or blue with gray eyes. Hazel eyes were also more common in rheumatic children, and both of these points held not only for the rheumatic group, but for the nonrheumatic members of rheumatic families. The control group (in Toronto) showed a higher proportion of children with clear blue eyes. The numbers of children with definitely brown eyes were about equal in both rheumatic and nonrheumatic families. The families of rheumatic children tended, therefore, to be lighter haired and more frequently red-haired than those of nonrheumatic children. There was a preponderance of blue-yellow and hazel eyes.

TABLE 7.—*Occurrence of Simultaneous Attacks of Rheumatism in a Family*

Toronto	Total Attacks	St. Louis	Total Attacks
Simultaneous attacks, 51 instances..	127	Simultaneous attacks, 30 instances..	71
Apparently unrelated.....	267	Apparently unrelated.....	118
	394		189

OCCURRENCE OF SIMULTANEOUS ATTACKS OF RHEUMATISM IN A FAMILY

The attacks that occurred were divided into two groups: (*a*) the group in which two or more members were simultaneously in bed with rheumatism; this included several attacks occurring up to eight weeks after the patient with the initial attack became sick; (*b*) the group in which attacks occurred not simultaneously but in persons with considerable contact. All attacks of parents during childhood were excluded in this study, and only parental attacks occurring during the life-time of the children were included.

These findings are summarized in table 7.

The number of persons having attacks at any one time varied in St. Louis between two and four; in Toronto, between two and six.

It was felt that in the second group (group *b*) many of the attacks occurred sufficiently closely to have been considered as "simultaneous." It has been shown experimentally by studies of the fibrinogen content of the blood, and it has been noted clinically, that rheumatism, like tuberculosis, may remain latent for long periods and then recur.

THE OCCURRENCE OF DISEASES OTHER THAN RHEUMATIC IN RHEUMATIC AND CONTROL GROUPS

Infections.—During the work on this study it was felt that writers on the subject who believed rheumatism to be contagious had not studied the other infections to which rheumatic subjects were prone sufficiently to rule out a general susceptibility to infections as an explanation for the increased susceptibility to rheumatism.

A study was made of the other infections occurring in rheumatic and control subjects, and for brevity they will be tabulated only as infections of the upper respiratory tract (colds and sore throats) and pneumonias. It will be seen (table 8) that three groups were studied, consisting of: (*a*) all the subjects in the rheumatic families, (*b*) the rheumatic subjects only and (*c*) the control group. The widest variations occurred in these groups, as will be seen.

Thus the entire group of people represented in the rheumatic families was more subject to colds and sore throats than the general population as

TABLE 8.—*Occurrence of Infections in the Rheumatic and the Control Groups*

	Colds, per Cent	Tonsillitis, per Cent	Pneumonia, per Cent
Entire family of rheumatic subjects	58	52	6.5
Rheumatic subjects only	88	80	12
Control subjects	24.5	18	3

represented by the control group. It was also found that during the inquiry as to simultaneous attacks of rheumatism previously referred to, numerous definite instances were cited in which pneumonia, tonsillitis or nephritis occurred in one member of a family, while rheumatism occurred in another.

Other Conditions.—A comparison of the occurrence of allergic symptoms, asthma, eczema (infantile) and hay fever was also made in the various groups in the two clinics. It was found that an identical percentage of allergic subjects existed in (*a*) the rheumatic group, (*b*) the nonrheumatic relatives of rheumatic subjects and (*c*) the control group. There is thus no reason to associate the presence of the allergic syndrome with rheumatism.

Thyroid dysfunction has been suggested by Langdon Brown [6] as having an association with rheumatism. Our figures tended to confirm this, since the percentage of rheumatic subjects with clinical thyroid disease (simple enlargement, colloid goiter, toxic goiter) was twice that of the nonrheumatic subjects with the same condition. The figures on the latter point represent only the Toronto clinic.

6. Brown, W. Langdon: Lancet **1**:1018 (May 19) 1928.

COMMENT AND SUMMARY

No agreement has been reached by workers as to the relative importance of heredity (of which Draper is one of the chief exponents) and of contagion in the occurrence of rheumatism.

From the foregoing study the impression is confirmed that rheumatism tends to attack more than one member in a family. It has been shown that the incidence of multiple cases in families was about equal in Toronto and in St. Louis, but that the number infected per family was higher and the age of onset lower in Toronto. Simultaneous attacks were shown to be frequent. This might be taken as evidence in favor of the action of a specific infective agent, but the rest of the evidence was against such a view, and the fact itself is not incompatible with a quite different interpretation. It has been shown that rheumatism is more common in the more distant relatives of rheumatic families than in those of controls. It affected both of two pairs of identical twins simultaneously but only one of each pair of dissimilar twins. This condition was also commoner in the families in which the father was affected, which would surely not be the case if contagion were the prime factor. Rheumatism tended to occur in blond and red-haired persons, particularly in those with bluish-yellow or hazel eyes, but these characteristics were also found in the nonrheumatic relatives of those persons. The coloring thus had no bearing on the actual occurrence of rheumatism, but pointed to a type in which rheumatism frequently occurs.

The greater susceptibility of girls to rheumatism was found to be demonstrated chiefly in families in which the father was rheumatic, which was suggestive perhaps of the existence of a rheumatic-susceptible character that might be transmissible from father to daughter.

Because of many clinical resemblances between rheumatism and atopic hypersensitiveness, studies similar to those adopted by Cooke and Vander Veer and by Coca and Cooke were made. These, however, showed that apparently no relation existed between the amount of infection in the parents and the age of onset of rheumatism in the children, and that the proportion of the family affected was not greater when both parents are rheumatic. The short investigation into the blood groups of the families showed, as did Levine's work on atopy, that there was no evidence that the agglutinogens played any part in a hereditary transmission of disease.

The apparent susceptibility of rheumatic persons to other infections was striking, and must be taken into account in the drawing of conclusions about the nature of rheumatism. The belief that dysthyroidism is associated with rheumatism was confirmed.

CONCLUSIONS

From the foregoing evidence, the undoubted familial occurrence of rheumatism would seem to be due less to a specific and contagious agent than to certain familial characteristics which favor: (*a*) the onset of many infections and (*b*) the appearance of the syndrome known as rheumatism. The determining factor in rheumatism may be nonspecific, since other acute infections of a different nature may arise simultaneously with rheumatic manifestations. Simultaneous attacks of rheumatism would then be explained by some nonspecific but infective agent attacking several people of like "rheumatic" constitution. This is in keeping with the growing opinion of bacteriologists that rheumatism is a specialized type of reaction to a common infective agent.

Dr. Cecile Asher of Toronto and the staff of the Social Service Department of the two clinics, especially Miss Chamberlain and Miss Gambrill of St. Louis and Miss Kerr of Toronto, gave me constant help in obtaining the foregoing data.

LUNGS AFTER TREATMENT OF ASPHYXIA NEONATORUM IN THE DRINKER RESPIRATOR

REPORT OF THIRTY NECROPSIES

DOUGLAS P. MURPHY, M.D.

AND

JOHN T. BAUER, M.D.

PHILADELPHIA

Recent clinical reports by one of us (Dr. Murphy) dealt with the treatment of asphyxia neonatorum by means of the Drinker respirator.[1] This method of treatment was instituted because the infants, many immature, either failed to breathe spontaneously or gave only occasional feeble gasps. The same degree of negative pressure (equivalent to that of a column of water from 8 to 10 cm. high) was employed in all cases, but the duration of artificial respiration was not the same in any two, as treatment was continued until a normal type of breathing could develop. Thus many infants reacted favorably and survived the neonatal period. Yet, owing to severe asphyxia, the response in some infants was not satisfactory and death occurred despite treatment continued for some time after the circulation had ceased. On necropsy many of the infants who failed to survive were found to have been suffering from intracranial injury or other lethal complications. The present study was undertaken to find out whether any changes, occurring in the lungs of infants who died after such treatment, could be attributed to the use of the Drinker respirator.

From the Gynecean Hospital Institute of Gynecologic Research and the Ayer Clinical Laboratory of the Pennsylvania Hospital.

1. (*a*) Murphy, D. P., and Coyne, J. A.: The Use of a Modified Drinker Respirator in Treatment of Asphyxia Neonatorum, J. A. M. A. **95**:335 (Aug. 2) 1930. (*b*) Murphy, D. P.; Drinker, C. K., and Drinker, P.: The Treatment of Respiratory Arrest in the Drinker Respirator: A Clinical and Experimental Study, Arch. Int. Med. **47**:424 (March) 1931. (*c*) Murphy, D. P.; Wilson, R. B., and Bowman, J. E.: The Drinker Respirator Treatment of the Immediate Asphyxia of the Newborn, with a Report of 35 Cases, Am. J. Obst. & Gynec. **21**: 528, 1932; (*d*) Late Respiratory Failure of Immature Infants Treated Successfully in Drinker Respirator, Am. J. Dis. Child. **42**:1075 (Nov.) 1931. (*e*) Murphy, D. P., and Sessums, J. V.: Asphyxia Neonatorum: Its Causes and Treatment by Prolonged Artificial Respiration; Report of Sixty-Six Cases, Surg., Gynec. & Obst. **55**:423 (Oct.) 1932.

METHODS

Thirty infants from the obstetric services of Dr. Piper and Dr. Vaux at the Philadelphia Lying-In Hospital and the maternity department of the Pennsylvania Hospital and the obstetric service of Dr. Piper at the University Hospital were the basis of this study. These infants, either failing to breathe or breathing very feebly at birth, had been given artificial respiration in the Drinker respirator, but died within twenty-four hours after birth. Whenever possible, a postmortem examination was made, including that of the skull and brain, and portions of the lungs were taken at random for histologic study. No special technic was employed in the preparation of the sections. As controls, sections of lungs from a similar group of infants who had not been treated in the Drinker respirator were examined. Some form of stimulus had probably been used to initiate breathing in the control infants, but its kind and duration were not mentioned in the clinical records. At the time of examination, in order to avoid prejudice, the sections of lungs from the infants treated in the Drinker respirator were mixed with those of the control

TABLE 1.—*Atelectasis in Relation to Respiration* *

Group	Respiration	Lungs Studied	Atelectasis				
			Present	Extent			
				Slight	Moderate	Marked	Complete
Treated in respirator	None	6	6	0	3	2	1
	Gasped only	10	9	0	2	6	1
	Eventual normal breathing	14	13	2	3	8	0
	Totals	30	28	2	8	16	2
Control	None	9	8	1	3	4	0
	Gasped only	4	4	0	2	2	0
	Eventual normal breathing	17	17	2	10	5	0
	Totals	30	29	3	15	11	0

* The incidence and approximate extent of atelectasis in treated and control infants who either were still-born or died within twenty-four hours after birth is shown, arranged according to the degree of spontaneous respiratory vigor. Note the high incidence of atelectasis in both the treated and control groups, and the greater frequency of the more widespread atelectasis in the treated patients.

group, and the one of us (Dr. Bauer) who made the examination had no previous knowledge of (1) the clinical conditions, (2) the gross postmortem findings or (3) the final pathologic diagnosis in any of the cases. The degree of aeration and atelectasis, the nature of the contents of the alveoli and bronchi and the presence and location of hemorrhages were noted. The extent and severity of these changes were estimated.

RESULTS

Gross Pathologic Changes in Lungs and Pleura.—The pleural cavities of both groups of infants showed nothing unusual. Subpleural petechial hemorrhages were seen frequently. No overdistention of the superficial alveoli was noticed; instead, varying degrees of atelectasis existed in many places in the lungs.

In the lungs of two infants treated in the respirator and two untreated infants who were never supposed to have gasped, there was evidence of slight aeration. Nevertheless, the amount of aeration was generally in proportion to the degree of spontaneous respiratory vigor.

Microscopic Observations in the Lungs and Pleura.—Pulmonary Expansion: On the basis of the clinical history, the infants treated in the respirator were divided into three groups: (1) those who failed to breath, (2) those who gasped a few times but in whom a normal depth or rate of breathing never developed and (3) those in whom normal breathing developed but who died within twenty-four hours of birth.

In the examination of one or more sections of the lungs of each infant, no alveolar overdistention was noted. There were no signs of injury which could be attributed to overexpansion of the lungs, induced by the negative pressure applied by the respirator to the thoracic wall of the infant. The incidence and relative extent of atelectasis is shown in table 1. In both groups the incidence of atelectasis was approximately the same, but when present, it was a trifle more extensive in the lungs of the infants treated in the respirator. This difference probably was not significant, since the whole of each lung was not examined.

TABLE 2.—*Contents of Air Passages* *

Infants	Number of Lungs Studied	Solid Particles	
		Bronchi	Alveoli
Treated in respirator	30	17	28
Control	30	13	27

* The incidence of solid particles as seen microscopically in the bronchi and alveoli of treated and untreated infants. Note the similarity in the incidence of particles in the two groups, and the constant relation between the numbers seen in the bronchi and alveoli of each group.

Contents of Alveoli and Bronchi: In experiments on asphyxiated cats, treated in the respirator with the head below the level of the chest, the pharyngeal and upper bronchial contents apparently were not drawn deeper into the bronchi against the force of gravity.[2] Since the infants were treated in the same relative position and with the same degree of force, it seemed unlikely that their alveolar and bronchial contents should have been influenced by the action of the respirator. Only occasional evidences of free fluid were seen in the bronchi and alveoli. This may have been present before respiration was begun, or it may have collected there terminally as a result of a failing heart or through regurgitation of material from the esophagus. The frequency with which alveolar and bronchial contents were found is shown in table 2. Amniotic débris was the material seen most frequently in the alveoli and bronchi (table 3), and the presence of this suggested inspiratory movements before birth. When comparing the relative frequency with which débris was noted in the alveoli and bronchi of the two groups of infants (table 3), it seemed as if more débris had collected in the alveoli and

2. Unpublished data.

less remained in the bronchi of the infants treated in the respirator. No marked differences were seen, however, although the respirator was probably more effective in drawing this material from the bronchi into the alveoli than the other, unknown, respiratory methods used in the control group.

Red blood cells, which were a result of either the aspiration of blood or intrapulmonary hemorrhages, occurred next in frequency in the alveoli and bronchi. As the incidence was the same in both groups, there was no evidence that the Drinker respirator was a causative factor.

TABLE 3.—*Bronchial and Alveolar Contents* *

Nature of Material	Thirty Treated Infants		Thirty Control Infants	
	Alveolar Contents: No. Infants	Bronchial Contents: No. Infants	Alveolar Contents: No. Infants	Bronchial Contents: No. Infants
Amniotic débris	22	8	18	11
Red blood cells	14	8	15	6
White blood cells	7	1	4	1
Edema	4	0	3	0
Mononuclear leukocytes	2	0	4	0
Fibrin	0	0	1	0
Desquamating epithelial cells	0	0	1	3

* The character and the relative frequency of the various cellular elements observed microscopically in the alveoli and bronchi of the treated infants are compared with those found in the control group. Note the parallelism between the two groups with respect to the relative frequency of the more commonly found cellular elements and also with regard to the location of these elements in the alveoli and bronchi.

TABLE 4.—*Microscopic Evidence of Pulmonary Congestion* *

Treatment	Lungs Studied	Congestion			
		Present	Degree		
			Slight	Moderate	Marked
Respirator	30	27	10	11	6
Control	30	22	8	9	5

* The incidence and degree of pulmonary congestion observed microscopically in the lungs of infants who were given artificial respiration in a Drinker respirator are compared with the observations in the control group of infants. Note the higher incidence of congestion in the treated group, and the approximate parallelism with respect to the degree of congestion in both.

Pulmonary Congestion: Venous congestion was slightly more frequent in the treated than in the control group, but the differences in degree seemed hardly significant (table 4). The degree of congestion had no relation to the degree of respiratory vigor of the infant.

Subpleural Hemorrhages: Subpleural petechial hemorrhages, lesions that often occur in asphyxiated infants, were no more frequent in the treated than in the control infants.

Causes of Death.—The causes of death arranged according to their frequency and with respect to the use of the Drinker respirator are shown in table 5. It is evident that prematurity and intracranial injury were responsible for approximately 70 per cent of the deaths. In only

one case could a pulmonary cause of death be found. This was pneumonia and occurred in one of the controls. The presence of atelectasis, mentioned as a probable cause of death in one infant, cannot be considered a pathologic change resulting from artificial respiration, but rather a condition due to a lack of respiratory effort or vigor. In four instances in which the cause of death could not be determined at necropsy, no pulmonary lesions were found. In no case, therefore, was the use of the Drinker respirator attended by a pulmonary lesion of sufficient gravity to be the cause of death.

COMMENT

The infants forming the basis of the present report were treated uniformly with a negative pressure not exceeding from 8 to 10 cm. of

TABLE 5.—*Causes of Death* *

Cause of Death†	All Cases	Artificial Respiration	
		Applied	Not Applied
Prematurity	22	13	9
Intracranial injury	20	11	9
Undetermined	4	3	1
Injury to umbilical cord	3	1	2
Syphilis	2	0	2
Hemorrhage into spinal cord	1	1	0
Eclampsia	1	1	0

* The chief pathologic causes of death in a group of thirty infants who were subjected to artificial respiration in a Drinker machine are compared with those in a similar group of untreated infants. Note the high incidence of prematurity and intracranial injury in both groups. Furthermore, note that only two deaths were deemed pulmonary in origin and that these occurred in the group of untreated infants.

† The seven remaining patients in the control group died from: (1) prolonged labor, (2) premature separation of the placenta, (3) difficult delivery, (4) pneumonia, (5) atelectasis and (6 and 7) fetal abnormalities.

water. These levels of pressure were selected as a result of experiments in which cats were rendered apneic by intravenous injections of curare and then kept alive by artificial respiration in a Drinker machine. Various degrees of negative pressure were employed in this manner, a constant pressure being maintained for each animal. At the end of each experiment, their lungs were examined for evidence of injury. At levels of 8 or 10 cm. of water pressure, no injury of the lung was seen, nor was any noted at somewhat higher levels, if the bronchial tree was clear of mucus. If the latter was present in a large amount and if levels of pressure above 15 cm. were employed, sharply marginated areas of atelectasis and hemorrhage were not infrequently observed. Emphysema, varying chiefly in degree and slightly with the duration of the treatment, was seen also at the higher levels. In some cats, considerable gross pulmonary congestion was present after more vigorous and prolonged periods of treatment. At excessive pressure (from 35 to 45 cm.

of water) the whole lung presented massive hemorrhages through rupture of alveolar walls.[3]

The present series of observations is small and the method of microscopic study was somewhat crude because examination of many sections of representative areas of the lungs was not possible. In spite of these limitations, even though a more accurate method of evaluating differences was not possible, we are of the opinion that the Drinker respirator, used with a recurring negative pressure of 8 or 10 cm. of water, exerted no deleterious influence on the infants, regardless of the duration of the treatment, which in some instances amounted to several hours.

In view of the causes of death, chiefly prematurity and intracranial injury, a beneficial effect from any method of artificial respiration was hardly to be expected. However, if atelectasis were the only pathologic condition considered, it is suggested, on the basis of the experimental work on cats and the degree of persistent atelectasis in this series of infants, that the negative pressure could be raised to 15 cm. of water without injury to the lungs. From some personal measurements made recently by one of us (Dr. Murphy) on the movement of air in deeply asphyxiated infants treated in the respirator it seems probable that a positive pressure equal to the negative pressure should be used to replace that of the atmosphere which in the past was alternated with the negative pressure produced by the respirator. Such an addition, together with the use of 15 cm. of pressure instead of 10 cm., may prove more beneficial in resuscitating asphyxiated new-born infants in the Drinker respirator.

SUMMARY AND CONCLUSIONS

1. The pathologic changes in the lungs of thirty asphyxiated infants who were given artificial respiration in the Drinker respirator, but who died within twenty-four hours after birth, are compared with those in a similar number who had not received this means of artificial respiration.

2. Seventy per cent of these thirty deaths were the result of either intracranial injury or prematurity. There was no death due to a pulmonary condition.

3. A slight increase in the incidence of pulmonary congestion followed the use of the Drinker respirator; this indicated that the treatment had an appreciable effect on the contents of the chest.

4. Artificial respiration had no influence on the kind of cellular elements observed in the air passages, but may have drawn amniotic débris from the bronchioles to the alveoli. Otherwise no gross or microscopic changes were recognized in the lungs of the treated infants that had not been seen in the lungs of untreated infants.

3. Murphy, Drinker and Drinker.[1b] Unpublished data.

5. In no case was any injury done to the respiratory tract by the use of the respirator.

6. In view of these findings, when asphyxia is due to atelectasis it is probable that the previously used 10 cm. of negative pressure can be raised safely to 15 cm. Furthermore it may be advisable to alternate this higher degree of negative pressure with an equal amount of positive pressure, instead of with atmospheric pressure, as has been used as a routine measure in the past.

STANDARDS OF BASAL METABOLISM FOR CHILDREN OF RETARDED GROWTH

ANNE TOPPER, M.D.
NEW YORK

Many workers studying the metabolism of children have found that their figures vary a great deal, depending on the prediction standards used. Until Benedict and Talbot [1] published their studies on the metabolism of normal children, there were no reliable normal standards in childhood. The tables published as a result of their work are useful in predicting the basal heat production of the average child.

The prediction standards available are for total calories referred to body weight, total calories referred to surface area and total calories referred to age. In addition, Benedict [2] recommended a standard referred to total height, which has been worked out by Talbot [3] for growing children. Pirquet [4] found that the sitting height bears a fairly constant relationship to body weight and to total metabolism, and he suggested a formula based on sitting height which my associates and I found to be an excellent single standard.

These five standards of basal metabolism—total calories referred to height, to sitting height, to weight, to surface area and to age—seem to bear a fairly constant relationship to the total metabolism of normal children, most of the children conforming within 10 per cent above and below the hypothetic line indicating the general trend of the predicted basal metabolism. There seems to be a distinct correlation between total basal metabolism and body measurements—stature, sitting height and surface area—and also between total metabolism and body weight and total metabolism and age. A detailed discussion of all these standards may be found in Benedict and Talbot's monograph on "Metabolism and Growth from Birth to Puberty." [1] Even the obese child and the thin child seem to fall within the limits of normality, and for the average child, any of these standards may safely be used. It is wise, however, to use all available standards for comparison with the observed basal metabolism in order to obtain a complete picture.

From the Pediatric Service of Mount Sinai Hospital.

1. Benedict, F. G., and Talbot, F. B.: Metabolism and Growth from Birth to Puberty, Washington, D. C., Carnegie Institution, 1921, no. 302.

2. Benedict, F. G.: Am. Philos. Soc. **43**:25, 1924.

3. Talbot, F. B.: Physiol. Rev. **5**:477, 1925.

4. Pirquet, C.: An Outline of the Pirquet System of Nutrition, Philadelphia, W. B. Saunders Company, 1925.

During the course of the past few years, it was found that a real discrepancy existed only in the case of the child who was retarded in growth, but was normal in other respects, and the purpose of this paper is to present studies on the basal metabolism of twenty such children.

Basal Metabolism of Children Retarded in Growth; Essential Data

Column 1	2	3	4	5	6	7	8	9	10	11	12	13
								Prediction Standards of Basal Metabolism Total Calories Referred to				
Case*	Date	Age, Yrs.	Ht., Cm.	Sitting Ht., Cm.	Wt., Kg.	Surface Area, Sq.M.	Total Calories Observed	Sitting Ht.	Total Ht.	Wt.	Surface Area	Age
1. E. R. ♀	8/27/29	7	76	46	7.7	0.45	820	423	557	450	480	820
	3/15/30	8½	96	56	17.4	0.60	912	627	644	735	640	900
	11/15/30	9	103	57	20.0	0.70	960	650	700	800	730	940
	3/24/32	10½	114	64	23.4	0.84	1,037	819	807	880	850	1,020
2. P. V. ♂	11/21/29	8½	111	61	20.0	0.78	1,046	744	840	870	830	1,015
	5/23/30	9	114	64	21.0	0.80	1,099	819	865	900	850	1,030
	11/24/30	9½	117	65	22.0	0.85	1,123	845	895	920	900	1,050
	3/24/32	11	127	70	25.0	0.94	1,231	980	1,015	1,000	980	1,130
3. S. L. ♀	5/17/32	8½	100	58	15.0	0.65	912	673	675	680	680	900
4. S. S. ♀	4/12/30	12	124	67	28.0	1.00	1,104	898	905	1,000	980	1,050
5. M. G. ♀	5/11/32	10	116	63	19.5	0.75	974	794	828	800	760	975
6. A. B. ♀	12/ 7/29	10	117	64	22.0	0.84	1,037	819	837	860	850	975
7. A. C. ♀	12/14/29	9	116	63	21.0	0.82	950	794	828	830	825	925
8. U. G. ♀	12/ 7/29	9	115	63	19.5	0.75	950	794	817	780	760	925
	12/15/30	10	118	64	22.0	0.84	1,000	819	847	860	850	975
9. H. C. ♂	4/ 8/30	12	128	67	26.5	0.96	1,226	898	1,025	1,030	980	1,200
	5/ 7/32	14	131	70	28.0	1.00	1,300	980	1,060	1,080	1,020	1,300
10. S. G. ♀	10/16/30	9	95	55	15.0	0.63	930	605	637	690	650	930
11. N. W. ♂	11/12/31	5½	90	56	20.0	0.67	777	627	705	870	750	790
12. H. T. ♂	6/17/27	7	101	59	16.6	0.67	860	696	785	775	750	900
	6/23/28	8	104	60	17.5	0.71	900	720	800	800	780	950
	6/22/29	9	108	61	18.4	0.73	950	744	820	830	800	1,000
13. M. B. ♂	5/ 9/28	9	118	64	23.5	0.87	1,030	819	910	950	920	1,020
	4/ 3/29	10	124	66	25.5	0.92	1,100	871	980	1,000	960	1,080
	10/ 4/30	11½	128	67	26.0	0.95	1,200	898	1,025	1,025	980	1,180
14. W. L. ♂	5/ 9/28	11	114	64	21.5	0.82	1,157	819	865	900	860	1,130
15. A. H. ♂	9/ 5/30	8	110	60	17.5	0.75	929	720	830	800	820	950
16. J. N. ♂	11/10/31	8	110	62	17.0	0.74	950	769	830	800	800	975
17. M. Z. ♂	3/11/28	8	110	59	18.0	0.75	948	696	830	820	820	975
18. P. S. ♂	2/10/29	9½	110	63	21.0	0.79	1,050	794	820	900	850	1,050
19. W. G. ♂	3/ 9/31	5½	90	56	15.0	0.62	806	627	705	725	700	780
	4/ 3/32	6½	95	58	15.5	0.65	850	673	745	740	740	825
20. A. R. ♂	10/13/26	11½	127	70	30.0	1.00	1,188	980	1,015	1,040	980	1,130

* In this column, ♀ indicates female; ♂, male.

The accompanying table gives the essential data in these studies. The surface area (column 5) was computed from the DuBois body surface chart as prepared by Boothby and Sandiford (chart 1). The prediction standard based on sitting height (column 9) was computed from Pirquet's formula: "total calories equals the sitting height squared times 0.2 calory." In chart 2, the hypothetic line shows the trend of the basal metabolism plotted according to this formula.

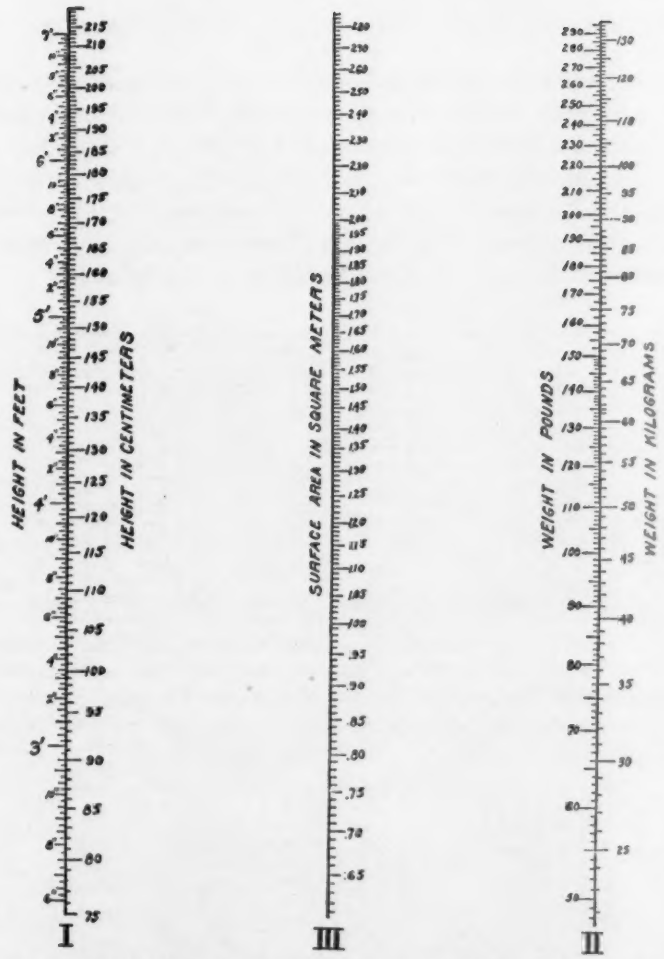

Chart 1.—DuBois body surface chart (as prepared by Boothby and Sandiford). To determine the surface area, draw a line through the height found in column *I* and through the weight in column *II*. Where this line intersects column *III* will be found the surface area in square meters. (Reproduced from DuBois: Basal Metabolism in Health and Disease, Philadelphia, Lee & Febiger, 1927, p. 120.)

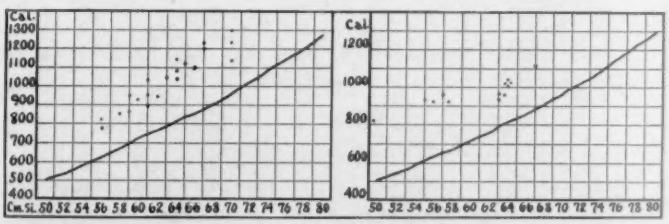

Chart 2.—The curves represent the general trend of the basal metabolic rate according to the Pirquet formula: sitting height times 0.2 calories. The dots represent actual basal metabolism in individual cases of the present series. Note how high the basal metabolic rate is in these cases compared to the Pirquet standard. In this chart and charts 3 and 4, the curve on the right indicates the total calories referred to sitting height in boys; that on the left, in girls.

The prediction standard based on total height (column 10) is plotted in chart 3 as a line showing the general trend of metabolism in children.

The total metabolism referred to body weight (column 11) is reproduced from Talbot's charts [5] in chart 5.

The total calories referred to surface area (column 12) is reproduced in chart 4 from Benedict and Talbot's monograph,[1] as are the graphs in chart 6—total calories referred to age (column 13).

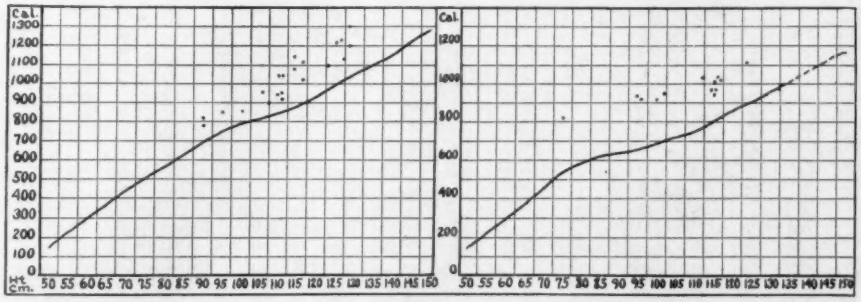

Chart 3.—The curves represent the general trend of the basal metabolic rate plotted from Talbot's tables based on height alone. The dots represent the actual basal metabolism in the present series. Note how high the basal metabolic rate is in these cases compared to the Talbot standard.

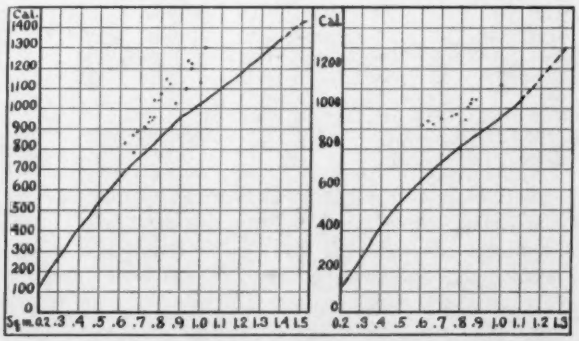

Chart 4.—The curves represent the general trend of the basal metabolism predicated from the DuBois surface area formula. The dots represent the actual basal metabolism observed in the present series. Note how high the basal metabolic rate is in these cases compared to surface area standard.

COMMENT ON CASES

E. R. (case 1) was studied for four years. On her first admission to the hospital, she was treated for celiac disease and was apparently

5. Talbot, F. B.: Standards of Basal Metabolism in Normal Infants and Children, Am. J. Dis. Child. **21**:519 (June) 1921.

cured; since then she has been followed in the outpatient department. She has remained well and normal, except for her greatly retarded growth. At the age of 7, her height, 75 cm., was 37.5 cm. less than the average height for the short child of that age.[6] At the age of 8, her height was 22.5 cm. less than her expected height. At 9 years, she was 20 cm. shorter than normal; at 10 years of age, she is 12.5 cm. shorter than the normal height for her age. Her metabolism has always

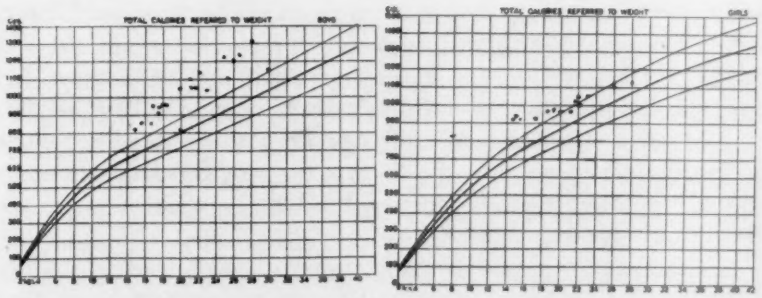

Chart 5.—The center curve indicates the general trend of the basal metabolism at the different weights of the Benedict and Talbot series. The curve is projected from 32 Kg. upward. The upper and lower curves represent the 10 per cent deviation above and below the normal. The dots represent the actual basal metabolism observed in the present series. Note how high the basal metabolic rate is in these cases compared to the Benedict and Talbot series.

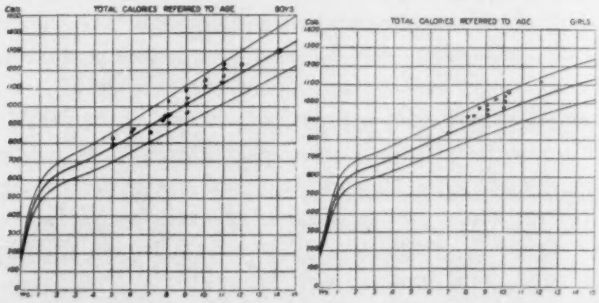

Chart 6.—The center curve indicates the general trend of the basal metabolism at the different ages of the Benedict and Talbot series. The upper and lower curves represent the 10 per cent deviation above and below the normal. The dots show the actual basal metabolism observed in the present series. Note that all cases in the present series fall within normal limits.

been abnormally high according to all standards, except the total calories referred to age. There were never any other signs of increased thyroid function, and we concluded that her basal metabolic rate was essentially

6. All figures for height were taken from the Baldwin-Wood weight-height-age tables prepared by R. M. Woodbury and published by the American Child Health Association, in Mother and Child, July, 1923.

normal, but that she simply did not fit into any known standards, except when referred to age, because of her abnormally retarded growth.

P. V. (case 2) was studied for four years. His blood picture, because of a high eosinophilia (68 per cent) and a palpable liver and spleen, suggested that we were dealing with a blood dyscrasia, and the seemingly high basal metabolism tended to confirm that diagnosis. The boy has remained well physically; his eosinophils are now down to 14 per cent; the liver and spleen are not palpable, and he seems normal in all respects except for his retarded growth. At the age of 8 years, he was 9 cm. too short for his age; at 9 years, 10 cm. less than his expected height; at 10 years, 11 cm. too short, and at 11 years, he is only 5 cm. less than the expected height for his age. His basal metabolic rate has always been high according to all standards, except the total calories referred to age. As the discrepancy between his height and his expected height becomes less, the basal metabolism seems less abnormal according to all other standards.

The patients in cases 8, 9, 12, 13 and 19 were followed in the outpatient department for one year or longer. These children are bright mentally, and physically they have always been normal in all respects except for their abnormally short stature and a basal metabolic rate that seems high by all standards except the total calories referred to age.

The rest of the children were studied over a shorter period. Many preliminary tests on metabolism were made until we were convinced that the seemingly high figures obtained were really basal. These children are normal in every respect except for their short stature and a basal metabolic rate that seemed high by all standards except the total calories referred to their age, and we must conclude that they have a normal basal metabolism which does not conform to any of the other standards.

To sum up, there were twenty normal children [7] who were from 5 to 37.5 cm. shorter than the shortest expected height for the age. Practically all the tests made on metabolism showed figures that exceed the 10 per cent limit of normality by all standards except the total calories referred to age. This may be seen from charts 2 to 6, in which the individual tests are shown as dots that are, in nearly all cases, above the line, showing the general trend of normal metabolism, except in charts 6, the total calories referred to age, in which the dots all fall within the normal limits.

Does this mean that the total calories referred to age is a good standard of metabolism? In a general way, the metabolism increases with age in childhood. Benedict and Talbot suggest that this may

7. The patients in cases 1 and 2, although not considered altogether normal children, seem to fit in with this group. Case 2 is being further studied by Dr. Bass.

merely be an expression of the fact that as children grow older, they grow heavier, and the larger the organism, the greater is the heat production. Normally, the total calories referred to weight, to body surface, to height or to sitting height would be more representative of the expected metabolism of the normal child than the total calories referred to age. In the short but normal child, however, Schick [8] has suggested that it is conceivable that while all physical characteristics—stature, weight, surface area and sitting height—are retarded in development, all other body functions, the work of the inner organs (heart, liver, intestines and kidney), have kept pace with the chronological age in their growth, and therefore in their cellular activity, and that as basal metabolism is an expression of the heat produced as a byproduct of cellular activity, there is a smaller disproportion between age and total metabolism in these cases than between physical surfaces and total metabolism. The basal metabolism in such cases is normal, but seems high because the cellular activity of the inner organs is accomplished at a seemingly greater expenditure of energy because of the reduced size of the body shell.

Practically, in evaluating tests on basal metabolism in such children, each child should be considered as a standard for himself, and all changes that may occur from time to time in the basal metabolic rate should be referred to his individual standard rather than to any general prediction standards now available. The greater the discrepancy between the expected stature and the actual stature of the child, the more abnormal will the basal metabolic rate seem to be when referred to any known standard, except, perhaps, total calories referred to age.

SUMMARY

The basal metabolism of children may be compared with prediction standards based on total calories referred to height, weight, sitting height, surface area or age. Most normal children fall within 10 per cent above or below the hypothetic line showing the general trend of metabolism (charts 2 to 6).

Studies on the basal metabolism of twenty children who were greatly retarded in growth but normal in all other respects are here recorded. The figures obtained do not conform to any of the standards usually used, except the total calories referred to age. The greater the disproportion between the actual stature and the expected stature for the age, the greater is the discrepancy between observed basal metabolism and expected basal metabolism by all standards except total calories referred to age.

8. Schick, Béla: Personal communication to the author.

Although normally this standard is not the best one, it is suggested that the reason underdeveloped children conform to this standard is that while their physical proportions have remained underdeveloped, the growth of the inner organs, and therefore the actual cellular activity of the body, has proceeded normally, commensurate with their age, the age being a truer measure of actual cellular activity and therefore of heat production than such body measurements as height, sitting height, surface area or weight.

In evaluating figures obtained from tests on the basal metabolism made on children who were much retarded in growth, each child should be considered as a standard for himself; changes in the metabolic rate that may occur from time to time should be referred to the individual basal rate of that particular child rather than to any known standards of metabolism, except perhaps that referred to age, as all other standards are too low for this type of child.

THE INTESTINE AND URINARY BLADDER IN POLIOMYELITIS

JOHN A. TOOMEY, M.D.
CLEVELAND

In a forthcoming paper[1] some reflex changes are described that occurred during the clinical course of poliomyelitis. Three hundred and eighty-six cases were studied during the past ten years. At the same time close attention was paid to the histories of upsets of the gastro-intestinal tract and urinary bladder, and all our patients were examined to discover especially the presence of neurologic involvements of either the intestine or the bladder. This paper contains an account of these studies.

THE GASTRO-INTESTINAL TRACT

It was difficult to determine beyond a doubt whether there was paresis or paralysis of the intestine, and, if there was involvement, where it was located. The difficulties can be appreciated when it is remembered that localized paralysis in the small intestine can exist without paresis or paralysis of the large intestine. The fact that there are evacuations of the lower intestine does not rule out the possibility of paralysis of the small intestine. Actual objective knowledge was meager, but inferential conclusions could be reached from available information.

The following criteria were adopted as significant of gastro-intestinal involvement: vomiting, pain in the abdomen and a history of obstinate constipation or diarrhea, all or any one of which was noticed at or before the onset of somatic paralysis. In 251 of the 386 cases there were such histories. The 17 abortive cases (included in the 251 cases) showed some gastro-intestinal reaction, evidenced chiefly by abdominal pain and diarrhea. In 45 of the 386 cases, the diagnosis of the outside physicians was "intestinal flu."

Such evidence, however, was only suggestive. Positive evidence was forthcoming when the parents or we ourselves tried to make the bowels move. It was noted by the parents of 51 patients that before voluntary muscle paralysis developed in their children there was something wrong with the gastro-intestinal tract, since neither enemas nor the ordinary cathartics would bring about an evacuation. After the patients were admitted to the hospital, the gastro-intestinal tract was

1. Toomey, John A.: Some Reflex Changes in Poliomyelitis, Am. J. Dis. Child., to be published.

examined in each instance. Enemas were given again and again to gage the activity of the lower intestine. When a paralyzed intestine was present, the saline solution flowed in and often was not returned. At the time of admission, this was the condition of the lower intestine in the 51 patients already mentioned and in 47 additional patients. In all, 98 patients had a toneless intestine, 51 before, and 47 others at the onset of, somatic paralysis. Whether the latter 47 had trouble with the intestine before the voluntary paralysis appeared could not be accurately determined from the histories, since a negative or positive history was merely the gage of the parents' intelligent interest in the child. It is probable that the intestinal paralysis existed before the somatic paralysis appeared. The rectal sphincter was toneless in only 6 cases.

In addition to the evidence mentioned, there was an absence of the auscultating gurgle in 104 of the 386 cases.

One can conclude from clinical evidence that the gastro-intestinal tract was more often involved than was apparent, and that this involvement occurred in most instances before or at the same time that the somatic paralysis appeared.

THE URINARY BLADDER

The urinary bladder was involved more often than the average physician realized, but the paralysis was overlooked because the overflow dribbling of the patient was accepted as normal by both parents and physicians. This was the more probable since one is apt to think of infantile paralysis in terms of paralysis of the voluntary muscles, and to pay no attention to the sympathetic or the parasympathetic systems.

Of the 386 patients admitted, 60 had disturbances of urinary excretion, usually manifested as complete paralysis. In 42 of these 60 cases, the paralysis had appeared before somatic paralysis occurred, and the condition was noted by the parents. Eighteen patients had urinary disturbance on admission to the hospital and, since the time of admission coincided with the somatic paralysis, it could be inferred that the paralysis of the bladder did not occur after paralysis of the voluntary muscles, although it may not have occurred before. Disturbances must have been present in 14 other cases, since the histories suggested trouble in urination.

Eleven additional cases were studied in the same way that Head and Riddoch [2] investigated the bladders of patients with transected cords.

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2. Head, Henry, and Riddoch, George: The Automatic Bladder, Excessive Sweating and Some Other Reflex Conditions in Gross Injuries of the Spinal Cord, Brain **40**:188, 1917.

The number of patients studied was limited for various reasons, but was sufficient to illustrate the unanimity of the response.

Local stimuli over the head of the penis caused no reaction, injection of saline solution, in the manner described by Head and Riddoch,[2] caused no autonomic contractions, and no oscillation appeared in the mercury of the attached U-tube in any instance after the bladder was filled. A most important finding was that in 8 of the 11 cases there was little or no effect on the urinary bladder, with contraction of the recti abdominalis when the patients lay on their backs. Deep breathing had no effect on excretion, pricking about the anal opening was insufficient to originate a response, and sponging of the lower part of the abdomen with cold water was ineffective. The normal capacity of the bladder could not be determined accurately, since it kept dilating with each added volume of saline solution. Dull pain was felt as the bladder was dilated, but with relaxation and the ingression of more saline solution, this sensation was somewhat blunted for a time, reappearing when more fluid was added, or when pressure was applied to the abdominal wall over the pubic symphysis. This pain was not acute, sharp, or lancinating. The impression was that the bladder would have dilated until it ruptured, provided we could have added enough saline solution, a result prevented by the overflow dribbling. Even with a catheter in place there was occasional dribbling about the instrument. In moderately involved bladders there would of necessity be a modification of these findings, but one thing was obvious, that in these severe cases there was a paralysis of the detrusor muscle.

The type of incontinence is important. Do the patients have retention with overflow dribbling, a passive type of incontinence? They do have retention and they do have overflow dribbling, but the mechanism is not that of simple passive incontinence, since it is probable that the vesical sphincter is involved, with loss of tonic activity of the neck as well as of the body of the bladder.

In conditions other than poliomyelitis, when both the sphincter and the detrusor were involved, so-called "paralytic incontinence" occurred, with urine dribbling without accumulation. Though there was paralytic incontinence in infantile paralysis, the paradoxical condition of the bladder filling and then overflowing also was present. There was a difference between the paralysis of the bladder of patients with cord transections and that associated with infantile paralysis, since in the bladder of the former some tone was present, while in the bladder of patients suffering from infantile paralysis, in the type of cases described, it was always absent. There was an accumulation here, though both the sphincter and the detrusor muscles were paralyzed; since most of the patients stay prone on their backs, accumulation occurred in a depen-

dent direction, causing the lax bladder to fill, and, because of its position, to buckle on itself at the bladder neck, so that even overflow dribbling was at times difficult. That there was paralysis of the sphincter was demonstrated by the lack of tone felt on passing a urethral sound. Again, if the patient stood up and the filled bladder was held back and splinted by the hand, so that the buckling kink of the bladder neck was ironed out, the bladder would immediately be emptied. It was obvious that cortical voluntary impulses could not be transmitted to the bladder when it was involved in this manner.

Was the bladder involved because of lesions in the anterior horn cells? That this was impossible may be easily seen when the innervation of the organ is studied. The detrusor muscles are supplied by the parasympathetic nerve from the second, third and fourth sacral nerves; the sphincter by the sympathetic nerve, from the twelfth thoracic and first and second lumbar, by way of the inferior mesenteric ganglions. In 7 of the 11 cases studied, there was no involvement of the muscles that receive their nerve supply from the last thoracic nerves, and the cremasteric reflex, which originates in the first and second lumbar nerves, was involved in only 3 of the 11 cases. The other cases showed normal responses. The paralysis of the detrusor muscle of the bladder was complete; yet in only 1 case was there paralysis of the somatic musculature from the same spinal segment, thus proving that the paralysis is peripheral, rather than central in origin.

The ability to urinate returns promptly, tone comes back and the detrusor muscles function again, often in less than three or four days, and rarely later than seven days after the patient's admission to the hospital, no matter how severe the attack. The recovery of the involved somatic muscles does not in any way parallel this return to function of the muscle of the bladder. Clinically, these patients are like animals with their pelvic muscles cut, the difference being that in the former recovery takes place promptly, while in the latter it takes at least from four to five weeks to establish an autonomic reflex.

The same observations hold true with regard to the intestines. Though paralysis of the small intestine exists, there is often no evidence of involvement of the muscles that receive their nerve supply from the same spinal somatic segment, i. e., the abdominal muscles chiefly.

COMMENT

On the basis of histories and of clinical and experimental facts, it would seem that the best explanation of the involvement of the urinary bladder and of the gastro-intestinal tract would be to suppose that it occurred during the logical and normal process of the accumulation of the toxin of infantile paralysis in the urinary bladder and

the gastro-intestinal tract. As a consequence of this accumulation, the gray fibers were involved wherever found, irrespective of system. With these points in mind and those brought out in a forthcoming paper,[1] there appears to be some evidence of the primary involvement of the autonomic nervous system.

CONCLUSIONS

1. The urinary bladder and the intestine were found to be frequently involved in cases of infantile paralysis.

2. This paralysis was usually noticed before, but was sometimes not noticed until after, somatic paralysis appeared.

3. Both lesions were peripheral, and not central.

CHEMICAL ALLERGY AND NIRVANOL SICKNESS

PRELIMINARY REPORT

BÉLA SCHICK, M.D.
HARRY SOBOTKA, PH.D.
AND
SAMUEL PECK, M.D.
NEW YORK

For the past five years one of us (Dr. Schick) has been studying the disease that follows the administration of nirvanol (phenyl-ethyl-hydantoin), the drug used so widely in the treatment of chorea. The name "nirvanol sickness" was originated by von Pfaundler, who compared the disease with serum disease. There exist in both diseases a time of incubation of similar duration, a fever, rash, edema, leukopenia with relative lymphocytosis, eosinophilia, swelling of the lymph glands and other symptoms. Other similarities were pointed out by Payne and de Rudder, such as an alkalosis during the time of incubation, which changes to acidosis at the outbreak of the rash.

According to the literature well developed nirvanol sickness improves the symptoms of chorea. Children show nirvanol sickness more frequently than do adults. Barbital and phenobarbital are also able to produce symptoms similar to those produced by nirvanol, although less frequently. Apparently, all of these drugs have two different effects: a pharmacologic effect, which is hypnotic, and a toxic effect, which shows in the fever and rash, as well as in other symptoms.

It is impossible definitely to prove the theory that nirvanol sickness is an allergic disease. The passive transfer of allergy by the method of Prausnitz and Küstner could not be obtained. There are other discrepancies between the two diseases. For example, it is rarely possible to produce nirvanol sickness with only one dose. Of course, each

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From the Pediatric Department and the Laboratories of Mount Sinai Hospital.

Read at a Meeting of the American Pediatric Society, Rochester, N. Y., June 27, 1932.

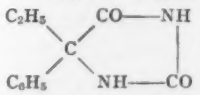
These studies were carried out with the support of an "Allergy Fund" donated anonymously.

The chemical part is discussed in the paper of Sobotka et al. (Sobatka, H.; Peck, S. M., and Kahn, J.: J. Biol. Chem. **97**:79, 1932; J. Pharmacol. & Exper. Therap. **47**:209 (Feb.) 1933. Sobotka, H.; Holzmann, M., and Kahn, T.: J. Am. Chem. Soc. **54**:4697, 1932), read at the Philadelphia Meeting of the American Society of Biological Chemists, April, 1932.

separate dose must be limited in size. With repeated administrations of nirvanol at intervals of two weeks or more, immediate reactions have been observed, but less frequently than in serum sickness. More often the reactions are of a lesser intensity or no reaction occurs, which indicates that an increased resistance rather than an anaphylaxis can result as a consequence of previous administrations.

Allergy following the administration of chemically well defined substances was studied by Bloch, Jadassohn and their pupils (primula poison, arsphenamine, etc.).

One of us (B. S.) thought that phenyl-ethyl-hydantoin



was well suited for studying its toxic effect, and discussed the problem with Dr. Sobotka, who discovered that nirvanol, as it is used, is a racemic mixture of levoform and dextroform. He was able to resolve the nirvanol into its two forms. These substances are optical isomers; they possess identical physical characteristics (solubility, melting point, etc.), but differ as to their influence on polarized light. The specific rotation is $(\alpha)_D + 119$ and $(\alpha)_D - 119$. Furthermore Sobotka succeeded in synthesizing both forms separately and independently.

As levorotatory substances frequently show more intensive biologic activity than dextrorotatory substances, it was of interest to use both forms of nirvanol in the treatment of chorea, especially with regard to their ability to produce the symptoms of nirvanol sickness and concerning their pharmacologic effect. The study of their pharmacologic effect when they were perorally administered to dogs and pigeons, intravenously to pigeons and subcutaneously to rabbits and rats showed that the effective minimum of the dextro-phenyl-ethyl-hydantoin lies a little less than 50 per cent higher than the minimum of the levoform. The difference between the levoform and the commonly used old nirvanol is within the limit of error.

Privatdozent E. Rothlin, Basel, carried out numerous pharmacologic tests on animals.

OBSERVATIONS

In the beginning of our study we treated twenty-five patients with chorea with the original nirvanol, which contains equal parts of the levoform and the dextroform. The daily dose was 0.3 Gm. It was given for from eight to ten days and was discontinued with the appearance of nirvanol sickness. Twenty-one patients, constituting 84 per cent, showed symptoms of nirvanol sickness, and four did not.

During the last two years we treated twenty-eight more patients, most of them having chorea and some epilepsy. Twelve of the patients were treated with the levoform and sixteen with the dextroform of

phenyl-ethyl-hydantoin. At the beginning of our study we did not know whether or not the levo-phenyl-ethyl-hydantoin alone produced the nirvanol sickness. We thought that the dextroform of phenyl-ethyl-hydantoin might have only a narcotic effect, and that it might not give rise to nirvanol sickness. The daily dose of levo-phenyl-ethyl-hydantoin was therefore reduced to 0.15 Gm., which amount equals the amount of levo-phenyl-ethyl-hydantoin present in 0.3 Gm. of the original nirvanol. We did not want to give double the amount of levo-phenyl-ethyl-hydantoin as a single daily dose, as this would have increased the intensity of the nirvanol sickness. It was only during the course of our study that we learned that dextro-phenyl-ethyl-hydantoin is also able to produce nirvanol sickness, although less frequently in the dose used. The daily dose of 0.15 Gm. of levo-phenyl-ethyl-hydantoin does not, therefore, correspond in its sickness-producing power to 0.3 Gm. of the original nirvanol. However, the results are interesting enough.

Whereas the administration of 0.3 Gm. of the old nirvanol resulted in sickness in 84 per cent of the cases, the twelve patients treated with a daily dose of from 0.15 to 0.3 Gm. of levo-phenyl-ethyl-hydantoin resulted in sickness in seven cases, no symptoms having occurred in five cases. However, among sixteen patients treated with dextro-phenyl-ethyl-hydantoin, sickness developed in only five, and eleven remained free from symptoms. We expect to find a higher incidence of nirvanol sickness with an increase in the dose of levo-nirvanol to 0.3 Gm. per day.

We do not want to discuss the therapeutic value of either the old nirvanol or the two new forms. We have the impression that a beneficial effect is achieved. The children treated with dextro-phenyl-ethyl-hydantoin also showed an improvement in the chorea, even without the development of a rash, which indicates that the rash and other symptoms of nirvanol sickness may not be essential for an effective treatment. It would be an advance in the treatment of chorea if we were able to dispense with the necessity of producing the nirvanol sickness.

The administration of nirvanol was repeated at given intervals in order to learn whether or not we would obtain an immediate reaction within twenty-four hours. The results were not uniform. One patient who showed nirvanol sickness after the administration of one dose of levo-phenyl-ethyl-hydantoin also had a rash and a rise in temperature after repeated doses of levo-phenyl-ethyl-hydantoin, but showed no symptoms after a dose of dextro-phenyl-ethyl-hydantoin. In three patients treated at first with one dose of dextro-phenyl-ethyl-hydantoin sickness again developed after repeated doses of the drug. Two of these patients also had an immediate reaction after a dose of levo-phenyl-ethyl-hydantoin. In two other patients the elicitation was unsuccessful.

We have not had much experience concerning the reelicitation of sickness in patients treated with old nirvanol. In one patient the readministration of 0.3 Gm. of old nirvanol fourteen days after the disappearance of the first disease was followed by an immediate reaction; in other cases, negative results were obtained. Several patients with chorea who were repeatedly admitted to the hospital and treated with old nirvanol showed, on the second administration of old nirvanol after an interval of from one to two years, sickness of either equal or less intensity. Other patients showed no symptoms. One child, in whom sickness did not develop during his first admission to the hospital, although eleven doses of 0.15 Gm. of nirvanol were administered, came down with symptoms during his second admission, but only after receiving twenty-two doses. Two cases are of interest, in which the children, having shown sickness after the administration of old nirvanol, developed immediate symptoms after the administration of phenobarbital. In other cases, such elicitation of sickness with phenobarbital could not be obtained.

The Prausnitz-Küstner passive transfer was attempted, but produced negative results in two cases.

COMMENT

It seems to us that we still have difficulties to overcome if we want to compare the mechanism of nirvanol sickness with that of serum sickness. We have to remember that in serum sickness we are dealing with a substance quite different from nirvanol. The injected horse serum circulates in the system in an only slightly reduced amount during the incubation period of serum sickness. Only a negligible amount is destroyed or excreted during this period. The diminution of the amount of the horse serum starts with the onset of the symptoms of serum sickness and continues during the sickness. On the other hand, with the administration of nirvanol, most likely a greater amount of it is excreted or destroyed before the nirvanol disease appears. Unfortunately, it is difficult to determine nirvanol chemically in the urine or the blood serum. The rate of excretion and destruction may influence the incidence of nirvanol sickness. This may also explain the differences or irregularities in the results of the readministration of nirvanol.

Of further interest is the observation that we were able to make concerning the localization of the nirvanol eruption at the site of positive reactions to tuberculin and diphtheria toxin. During the first days of intensive eruption, the region around these sites of positive reactions was spared a rash, and only on the succeeding days did the eruption invade this region. On the other hand, the eruption appeared around the site of the scratch of a negative test earlier.

In another case, the Pirquet test, made before the appearance of the eruption, gave a positive reaction, and when repeated twice during the eruption, each reaction was negative. After the nirvanol rash disappeared, the reaction became again positive. In this case, the appearance of the eruption in the region of the primarily positive Pirquet test was also delayed.

In conclusion, we wish to say that we have been able to show that old nirvanol is a mixture of a levoform and a dextroform of phenyl-ethyl-hydantoin, and that levo-phenyl-ethyl-hydantoin is more potent in producing sickness than dextro-phenyl-ethyl-hydantoin. This discovery permits us a more intensive study of the allergic features that may be present during nirvanol sickness. Some of these features, such as elicitation, have been discussed.

CONSTIPATION OF INFANCY

THE RECTAL FACTOR

HERBERT I. KALLET, M.D.
DETROIT

In reviewing the embryology of the gastro-intestinal tract, one notes that originally this is not a continuous canal. The primitive hindgut terminates as a blind sac called the cloaca, which is the anlage of certain genito-urinary as well as of intestinal elements. A plug of tissue, termed the anal plate, separates the cloaca from the ectoderm. The latter in turn dips inward, forming what is called the proctodeum. As the embryo develops, this plug is gradually absorbed, so that by the eighth week or earlier there is a complete union of the hindgut with the proctodeum.

Should arrest or distortion of this process occur, there results an anomaly or a malformation. These congenital defects are so spectacular that they present no diagnostic problem. It must be borne in mind, however, that while these malformations are rare, the line of fusion of the proctodeum with the entoderm in every new-born infant represents a point of natural stenosis. The sphincteric muscles are as yet rudimentary, and the anal orifice is a narrow, more or less fibrous ring.

In the normal infant, the lumen is large enough and the elasticity sufficient to permit the ready passage of the soft infant stool. In certain babies, however, this ring approaches the fetal type. The opening is exceptionally small and the elasticity minimal. In such cases the stool reaches the rectum and is expelled with great difficulty. At each defecation the child strains and screams as if in pain. Bowel movements are frequent and scant, or perhaps more commonly delayed. Nursing or the taking of water, which stimulates peristalsis, produces intestinal spasm, and the child is said to be suffering from colic. This colic is apparently not dependent on diet, and is found among nursing babies as well as in those given various formulas. The new mother, tired and weakened after her recent confinement, is often frantic, and is willing to try anything to ease the baby. Catnip and camomile, laxatives and soothing-syrup, pacifiers, peppermint and anything that a neighbor may suggest are employed, with little avail.

PROGNOSIS

Untreated, the condition tends in most cases to correct itself as the child becomes older. The growth of the parts and the development of the sphincteric muscles make the orifice larger and more elastic. With

the replacement of the infantile bowel movement by formed stools, the passage is mechanically dilated. However, the disturbed rest and the pampering during the early months that the so-called colicky baby receives often lead to bad habits and nervous conditions which are difficult to overcome. A tendency toward constipation is also established, which may be lasting. Furthermore, the straining serves to loosen the mucous membrane, which at best is not firmly attached. This tends to add to the mechanical block and may be the forerunner of rectal disease in later life. Fissures, too, are not uncommon, producing pain, spasm and bleeding.

TREATMENT

Treatment is extremely simple. With utmost gentleness the anus is dilated digitally. It is well to begin by using the small finger thoroughly lubricated, gradually changing to the index finger. It is important not to attempt to accomplish too much at one time. Usually two or even three treatments are necessary. Trauma must be avoided and instrumental stretching not attempted. It is well to follow the dilation by the instillation of some astringent to correct the tendency toward mucosal relaxation and to administer liquid petrolatum by mouth.

The results of these simple measures are striking. Within a few days, in cases of this type, bowel movements become normal and the colic ceases. Occasionally, it is necessary to repeat the dilation a few weeks later.

In only two instances, have I found it necessary to intervene surgically. Both of these patients were older babies in whom the stenoses were too severe to yield to dilation.

SUMMARY

1. The rectum of certain infants may approach the fetal type.

2. Stenosis of this kind may be a factor in constipation and colic of young babies.

3. A simple treatment by digital dilation is suggested.

944 Maccabees Building.

INFANTS BORN OF WOMEN HAVING TOXEMIA AS A COMPLICATION OF PREGNANCY

GEORGE CRAIG LUDLOW, M.D.
NEW YORK

The material for the present study was obtained from the records of the Manhattan Maternity and Dispensary, covering a period of six years (from 1921 to 1926, inclusive) and consisting of 148 cases. In order to evaluate the possible effect on the baby, it is necessary to understand the three types of toxemia which may occur in the mother. The classification used at this hospital and the number of cases in each group are as follows: preeclamptic toxemia, 92 cases; nephritic toxemia, 37 cases, and eclampsia, 19 cases.

TYPES OF COMPLICATION

Preeclamptic Toxemia.—This type, more frequent in primiparae but occasionally found in multiparae, occurs only in the latter half of pregnancy, and if not treated often leads to eclampsia. It is marked by a rise in the maternal blood pressure, with albumin and sometimes casts in the urine; these symptoms disappear shortly after delivery.

Of the 92 patients in this group, 33 were multiparae, but in only 3 cases had there been toxemia in previous pregnancies (2 stillbirths in eclampsia and 1 stillbirth in preeclampsia). There were 96 babies born, including 4 pairs of twins. Of the total number, 71 were born at term, and 22 prematurely; there were 1 abortion and 5 macerated fetuses. Of the 79 babies born alive, 65 were born at term and 14 prematurely. Seven autopsies were made, only 3 of which showed symptoms that could be ascribed to maternal toxemia. According to the pathologist's report, these were as follows: (1) macerated fetus, asphyxia and placental infarcts; (2) harelip, cleft palate and autolysis from maternal toxemia, and (3) maceration and autolysis from maternal toxemia. The 4 neonatal deaths showed nothing to suggest toxemia.

The average weight at birth of the babies born alive was 6 pounds, 4 ounces (2,800 Gm.), and their condition at birth was: good, 72; fair, 5, and poor, 2. Of the babies seen six weeks after birth, 50 were in good condition and 3 in fair condition, while 19 who were followed for only ten days after birth were in good condition at that time. The methods of feeding and the average gain are given in table 1.

Nephritic Toxemia.—This condition occurs more often in multiparae and may appear at any time during pregnancy, depending on the severity of the nephritis. When the renal lesion is slight, the ensuing eclampsia, if present, may be indistinguishable from that following preeclamptic toxemia, but when the lesion is marked, the eclampsia may resemble uremia (coma without convulsions). Clinically this type of toxemia is marked by the persistence of rise in blood pressure and by urinary casts and albumin after delivery. In the present group of 37 cases, 18 were multiparae, but there was only 1 record of toxemia in a previous pregnancy (stillborn child after induced labor in eclampsia). Of the total number, 17 were born at term, and 20 prematurely; there were 9 stillbirths, 1 abortion and 4 macerated fetuses. Of the 23 babies born alive,

TABLE 1.—*Methods of Feeding and the Average Gain in Infants of Mothers with Preeclamptic Toxemia*

No. of Babies	Method of Feeding	Average Gain in Six Weeks
46	Breast	2 lb., 3 oz. (985 Gm.)
23	Breast and bottle	1 lb., 1 oz. (528.4 Gm.)
8	Bottle	13 oz. (368.6 Gm.)

TABLE 2.—*Method of Feeding and Average Gain in Infants of Mothers with Nephritic Toxemia*

No. of Babies	Method of Feeding	Average Gain in Six Weeks
11	Breast	1 lb., 14 oz. (900 Gm.)
1	Breast and bottle	1 lb., 6 oz. (670 Gm.)
5	Bottle	1 lb., 10 oz. (783 Gm.)

11 were born at term, and 12 prematurely. In the 6 neonatal deaths, 5 of the babies were born prematurely and 1 at term; in none was there definite proof that maternal toxemia was a factor. Autopsies were performed on 11 babies, in 5 of whom there were definite signs of toxemia, as follows: (1) abortion and placental infarcts; (2) macerated fetus and placental infarcts; (3) stillbirth, infarcts and uterine asphyxia from maternal toxemia; (4) stillbirth and uterine asphyxia from maternal toxemia, and (5) stillbirth and placental infarcts.

The average weight of the babies born alive was 5 pounds, 3 ounces (2,385 Gm.), and their condition at birth was: good, 17; fair, 1, and poor, 5. At the end of the six weeks' supervision by the hospital, 16 babies were in good condition; 1, last seen on the tenth day, was also in good condition. The method of feeding and average gain are given in table 2.

Eclampsia.—Eclampsia usually occurs in primiparae, rarely appears in the first half of pregnancy and is influenced by lack of prenatal care. It is not infrequent in cases of twins or hydramnion. Clinically it is marked by the presence of convulsions before, during and after delivery.

Of the 19 cases in this group, 16 births, including 2 sets of twins, occurred in eclampsia following preeclamptic toxemia, and 5 in eclampsia following nephritic toxemia. There was only one record of eclampsia in a former pregnancy—a case of preeclamptic toxemia. In the first division (eclampsia following preeclamptic toxemia) 14 babies were born alive—11 at term, and 3 prematurely; there were 1 stillbirth and 1 macerated fetus. An autopsy on the neonatal death, that of a premature baby, showed no signs of toxemia. In the second division (eclampsia following nephritic toxemia) 5 babies were born alive; 4 at term and 1 prematurely, and there were no neonatal deaths. The average weight at birth of the infants born alive was 5 pounds, 5 ounces (2,441 Gm.). At the end of the six weeks' period of observation, 15 babies were in good condition and 1, not seen after the tenth day, was doing well at that time. The method of feeding and average gain are given in table 3.

TABLE 3.—*Method of Feeding and Average Gain in Infants of Mothers with Eclampsia*

No. of Babies	Method of Feeding	Average Gain in Six Weeks
8	Breast	2 lb., 6 oz. (1,070 Gm.)
8	Breast and bottle	1 lb., 11 oz. (811 Gm.)
2	Bottle	1 lb. (500 Gm.)

In all, 6 pairs of twins were born: 4 of mothers with preeclamptic toxemia, and 2 of mothers with eclampsia following preeclamptic toxemia. Five of these pairs made good progress, and the autopsy findings of the pair that died showed no definite evidence of toxemia.

Chemical examination of the blood of 15 mothers showed the lowest nonprotein nitrogen to be 23 mg., and the highest, 56 mg. The lower figures occurred, with a single exception, in preeclamptic toxemia, the highest in this group being 38 mg. The other cases were all in the nephritic group.

Wassermann tests of the blood were made in 100 cases, in only 2 of which the results were definitely positive. Thus it would seem that syphilitic infection had no part in the causation or course of toxemia.

A comparative analysis of the findings in the 3 groups of cases is presented in table 4.

It is difficult to draw full conclusions from this series, but obviously the babies of the mothers having nephritic toxemia have a poorer start and poorer prognosis than the other babies, as shown by: (1) the greater number of stillbirths, (2) the greater number of premature births, (3) the relatively weaker condition at birth of those born alive, (4) the higher neonatal death rate and (5) the relatively less satisfactory condition at discharge.

According to these observations, eclampsia is apparently not of great significance in its effect on the baby.

In regard to the general effect of toxemia on new-born babies, table 5 compares the babies of mothers having toxemia and the babies of normal mothers.

Analysis of the figures in table 5 show that babies born of toxic mothers do not, on the whole, have so good a start as those whose

TABLE 4.—*Comparative Analysis of Findings in the Three Groups*

	Toxemia of the Preeclamptic Type	Toxemia of the Nephritic Type	Toxemia Associated with Eclampsia
Babies born alive	79 (82% of 96)	23 (62% of 37)	19 (90% of 21)
Premature births	22 (23% of 96)	20 (54% of 37)	5 (24% of 21)
Condition of babies at birth:			
Good	72	17	16
Fair	5	1	2
Poor	2	5	1
Average weight at birth	6 lb., 4 oz. (2,813 Gm.)	5 lb., 3 oz. (2,385 Gm.)	5 lb., 5 oz. (2,441 Gm.)
Breast-fed babies	70%	60%	45%
Neonatal deaths	4	6	1
Autopsies showing definite signs of toxemia	3 (7 autopsies)	5 (11 autopsies)	0
Twins (6 pairs)	4	0	2
Condition on discharge (good)	72	17	16

TABLE 5.—*Babies of Mothers with Toxemia Compared with Infants of Normal Mothers*

	Babies of Toxic Mothers	Babies of Normal Mothers
Number of babies born	154	1,054
Born alive	121 (78.5%)	1,008 (95.6%)
Stillborn	21	28
Abortions	2	18
Macerated fetuses	10	0
Born at term	104 (67%)	1,003 (95.1%)
Born prematurely	50	51
Neonatal deaths	11 (8 premature)	28 (7 premature)
Twins	6 pairs 2 premature 5 did well	9 pairs 1 pair stillborn, premature 8 did well
Average weight at birth	5 lb., 9 oz. (2,555 Gm.)	7 lb., 9 oz. (3,455 Gm.)
Breast fed	58%	78%
Average gain, 6 weeks	1 lb., 6 oz. (670 Gm.)	1 lb., 12 oz. (840 Gm.)
Breast-fed	2 lb., 4 oz. (1,013 Gm.)	2 lb., 6 oz. (1,070 Gm.)
Breast and bottle	1 lb., 1 oz. (528 Gm.)	1 lb., 9 oz. (755 Gm.)
Bottle-fed	1 lb., 1 oz. 528 Gm.)	1 lb., 3 oz. (585 Gm.)
Condition at discharge, 6 weeks (good)	105 (86.6%)	985 (97.7%)

mothers are normal. The percentage of stillbirths, of twin births and of neonatal deaths is higher in the first group, while the average weight at birth and the average gain (as a whole as well as in each type of feeding) is higher in the babies of nontoxic mothers.

PREMATURE BIRTHS

Since many premature babies are born in these cases of toxemia, the additional comparative data on those born of mothers with and without toxemia should be of interest. The material consists of 138 babies born during four years (from 1927 to 1930, inclusive). Of this number 38, including 4 sets of twins, were born of toxic mothers, and 100, including 15 sets of twins, of nontoxic mothers. These figures show a slightly lower percentage of twins in the toxic group, which is perhaps of interest, since there is an impression that multiple births are prone to occur in cases of toxemia. The neonatal mortality of the twins is slightly higher (37.5 per cent) in the toxic than in the nontoxic group

TABLE 6.—*Condition at Birth and Death of Infants of Toxic and Nontoxic Mothers*

	Condition at Birth			
	Good	Fair	Poor	Deaths
Toxic group	15	15	8	6
Nontoxic group	45	38	27	36

(30 per cent). It was observed that although fewer babies in the toxic group were in good condition at birth, the neonatal death rate was decidedly lower than in the nontoxic group. While this cannot be offered as proof of the greater vitality of the toxic babies, it certainly suggests that the vitality is at least as good as that of the nontoxic babies. The statistics in table 6 explain the preceding statement:

Another interesting point is that although the toxic group contained only a slightly larger percentage of breast-fed babies, the average gain in weight in this group was strikingly better than that in the nontoxic group, and the breast-fed babies whose mothers had nephritic toxemia showed a better average gain (2 pounds, 5 ounces [1,041 Gm.]) in the six and one-half weeks period of observation than did the babies whose mothers had preeclamptic toxemia or eclampsia (2 pounds, 2 ounces [956 Gm.]). The breast milk used was frequently from nontoxic mothers, but most of the mothers with preeclampsia were able to nurse their own babies, as were a few of those with nephritis. The babies were given their own mothers' milk on the fourth or fifth day post partum, as it was considered that by that time most of the toxins would be eliminated. Breast milk from mothers with toxemia exerted no apparent ill effect on the babies receiving it.

Table 7 illustrates these points:

TABLE 7.—*Method of Feeding and Gain in Weight of Infants of Toxic and Nontoxic Mothers*

	Toxic	Nontoxic
Method of feeding:		
Breast	14	20
Breast and bottle	7	16
Bottle	10	30
Gain in weight (total average)	1 lb., 11 oz. (811 Gm.)	1 lb., 3 oz. (585 Gm.)
Breast-fed	2 lb., 4 oz. (1,013 Gm.)	1 lb., 5 oz. (641 Gm.)
Breast and bottle	1 lb., 10 oz. (783 Gm.)	1 lb. (500 Gm.)
Bottle	1 lb., 12 oz. (840 Gm.)	1 lb., 6 oz. (670 Gm.)

There were 23 autopsies performed, in only 1 of which any definite evidence of toxemia was found.

From these findings it may be assumed that the toxemia of the mothers has no particular deleterious effect on premature babies.

SUMMARY AND COMMENT

1. One hundred and forty-eight cases have been reviewed in an attempt to learn whether babies born of toxic mothers are in any way affected.

2. Comparative analyses are made of the effect on the baby in the three types of toxemia and on babies born of toxic and normal mothers.

3. A group of 138 premature babies (of toxic and nontoxic mothers) was also studied, and observations made with reference to the toxemia.

4. Babies born of toxic mothers do not have as promising a beginning as those born of normal mothers. Maternal nephritic toxemia usually means a poorer outlook for the baby than preeclamptic or eclamptic toxemia. Premature babies do not seem to be particularly influenced by maternal toxemia.

112 East Seventy-Fourth Street.

CUTANEOUS REACTION TO TUBERCULIN IN PRIMARY PULMONARY TUBERCULOSIS

GROWTH AND VARIABILITY OF SURFACE AREA

C. A. STEWART, M.D., PH.D.
MINNEAPOLIS

Allergic states resulting from tuberculous infections give rise to cutaneous reactions to tuberculin which in different persons vary tremendously in size and severity. These variations presumably parallel the degree of hypersensitiveness which the infections induce in the various tissues of the body. In other words, the severity of a cutaneous reaction probably is more or less directly proportional to the degree to which the necrotizing tissue toxicity of tuberculin is enhanced in the individual case.

In order to obtain information concerning the relative toxicity of tuberculin for different persons, a study of the surface area of the cutaneous reactions to this material (supplied by the Saranac Lake Laboratories) was undertaken on a group of Lymanhurst children (ranging from 8 to 14 years of age) all of whom had positive reactions to the Mantoux tests and calcified intrathoracic lesions typical of primary tuberculosis demonstrable by roentgen examination. In this group no cases were included in which the roentgenogram revealed the presence of either the acute inflammatory parenchymal stage of primary tuberculosis or the adult type of tuberculosis. This study, therefore, is confined strictly to children in whom repeated roentgenograms of the chest and examinations have justified one in considering that primary tuberculosis or tuberculosis of the childhood type was present in its late or healing stage exclusively.

Since the area of cutaneous reaction to the Mantoux test is frequently irregular in outline, it was considered desirable to employ a method of determination of the surface area which was more refined than one in which estimations are based solely on computations derived from measurements of the diameters of the zone of redness on the skin. A number of methods have been devised in the past for the measurement of irregular areas; among them may be mentioned the approximate graphical integration, the planimetric and the area-by-weight methods. In this study a modification of the area-by-weight method introduced originally by Hammar [1] was used. This method involved first a careful outlining with ink of the outer margin of the area of redness of the positive cutaneous reactions. A transparent celluloid composition was then placed over the area, and the outlined

From the Department of Pediatrics, the University of Minnesota.

1. Hammar, J. A.: Ztschr. f. ang. Anat. **1**:312, 1914.

margins marked on the skin were carefully retraced in ink on the superimposed paper. The field traced in this manner was then cut out with scissors and weighed on a delicate chainomatic balance. Lastly, the area of this cut out segment (which corresponded with the size of the area of the tuberculin reaction) was computed by dividing its weight by that of a sample of the same paper which had an area of 1 sq. cm.

This method is subject to certain sources of error, such as inaccuracies in tracing and cutting out the outlined areas and variations in the thickness, in the water content of the paper and in the static electrical charge. In order to obtain an approximate estimate of the magnitude of the combined error arising from these and other factors, twenty rectangular samples of the transparent paper were carefully measured and weighed. In measuring these samples a millimeter

TABLE 1.—*Showing Dimension, Area and Weight of Twenty Individual Samples of Transparent Celluloid Composition Paper and Weight Per Square Centimeter, Together with Totals, Averages, Mean Square Deviation, Standard Deviation and Coefficient of Variation*

Dimensions of Sample, Cm.	Area of Sample, Sq. Cm.	Weight of Sample, Gm.	Weight per Square Centimeter, Gm.
1.75 × 6.65	11.638	0.0733	0.00630
4.40 × 6.18	27.192	0.1716	0.00631
4.50 × 6.20	27.900	0.1754	0.00629
4.40 × 6.35	27.940	0.1823	0.00652
5.50 × 6.40	35.200	0.2312	0.00657
5.80 × 6.20	35.060	0.2150	0.00598
6.00 × 6.28	37.680	0.2342	0.00622
6.18 × 6.20	38.316	0.2367	0.00618
6.18 × 6.20	38.316	0.2389	0.00623
6.20 × 6.20	38.440	0.2354	0.00612
6.20 × 6.25	38.750	0.2350	0.00606
6.62 × 6.70	44.354	0.2751	0.00620
6.72 × 6.75	45.360	0.2785	0.00614
6.72 × 6.75	45.360	0.2891	0.00637
6.75 × 6.75	45.563	0.2835	0.00622
5.65 × 8.27	46.726	0.2937	0.00629
8.25 × 8.30	68.475	0.4179	0.00610
8.30 × 8.30	68.890	0.4241	0.00616
8.31 × 8.30	68.973	0.4275	0.00620
20.67 × 28.00	578.760	3.4870	0.00602
Total.....	1369.793	8.4054	
Average.....	68.4896	0.42027	0.00614
Standard deviation.....	.....	.....	0.000168
Coefficient of variation	.....	.....	2.74 per cent

scale was used; thus fractions of millimeters were estimated, and from the measurements obtained the area of each sample was computed. The weight of portions of the paper 1 sq. cm. in surface area, was then determined by dividing the weight of each sample by its computed surface area. According to the results obtained, which are recorded in table 1, the weight of a square centimeter of the paper was found to average 0.00614 Gm. (with a range of from 0.00598 to 0.00657 Gm.). The coefficient of variation for this series of twenty determinations amounted to ± 2.74 per cent. The inherent error involved in this method of determining the area of a positive reaction to the Mantoux test (± 2.74 per cent) is relatively insignificant as compared with the tremendous variations noted in the size of these areas in different persons. The method, therefore, was deemed sufficiently accurate to fulfil the requisites of the present study. In other investigations of irregular areas in which greater accuracy is required, one undoubtedly should determine the coefficient of variation from observation on small, as well as relatively large, samples

of paper selected at random. Further refinements may be obtained also by more careful measurement of samples selected, as well as by controlling their moisture content. Those interested in the technic of determining the area of irregular fields by various methods and the errors involved are referred to an excellent article by Scammon and Scott [2] dealing with this subject.

The present study is based on measurements of the area of the reactions recorded three, twenty-four, forty-eight, seventy-two, ninety-six and one hundred and sixty-eight hours following the intracutaneous injections of 0.1 mg. of tuberculin in sixty Lymanhurst children. In compiling the data, the individual cases were arranged in a progressive series with respect to the maximum area each tuberculin reaction attained, irrespective of the time at which the area of the skin reached

TABLE 2.—*Absolute (and Percentage of Maximum) Area Attained by the Mantoux Reactions at Various Periods, Together with Averages, Standard Deviations and Coefficients of Variation*

Groups of Ten Cases Each	Area of Reaction in Sq. Cm.						Percentage of Maximum Size at					
	3 Hrs.	24 Hrs.	48 Hrs.	72 Hrs.	96 Hrs.	168 Hrs.	3 Hrs.	24 Hrs.	48 Hrs.	72 Hrs.	96 Hrs.	168 Hrs.
1	1.61	6.91	6.21	5.15	2.91	0.82	23.2	100.0	89.6	74.3	42.0	11.8
2	1.12	14.8	20.3	14.6	6.8	7.6	5.5	72.9	100.0	71.9	33.5	37.4
3	3.3	17.8	29.4	17.4	7.3	4.5	11.2	60.5	100.0	59.2	24.8	15.3
4	2.9	21.3	33.6	29.2	14.4	4.3	8.6	63.4	100.0	86.9	42.9	12.8
5	1.9	27.1	41.2	25.8	13.2	6.6	4.6	65.8	100.0	62.6	32.0	16.0
6	3.7	31.0	61.8	66.4	38.5	10.5	5.6	46.7	93.1	100.0	58.0	15.8
Average of groups 1, 2, 3	1.6	13.2	19.0	12.6	5.8	5.0	8.4	69.5	100.0	66.3	30.5	26.3
Average of groups 4, 5, 6	2.8	26.1	47.1	40.5	22.7	7.0	5.9	53.4	100.0	86.0	48.2	14.9
Grand average	2.4	19.4	32.8	27.0	14.1	6.2	7.3	59.1	100.0	82.3	43.0	18.9
Standard deviation ± sq. cm.	2.7	10.5	18.6	29.1	26.0	4.4						
Coefficient of variation, ± per cent	112.5	54.1	56.7	107.8	184.4	71.0						

its greatest development. Averages were then determined for six successive groups, each of which included ten children whose reactions to tuberculin individually were larger or smaller in area than were the reactions noted for the cases included in the preceding or following groups, respectively (table 2).

The averages recorded in table 2 reveal that positive areas of reaction to tuberculin may attain appreciable size within three hours following the application of the test. At this period the mean areas for the different groups show considerable variability (a range of from 1.12 to 3.7 sq. cm., table 2), but the average is definitely larger for the thirty patients whose areas of reaction reached greater ultimate sizes than for the thirty children who were less allergic to tuberculin

2. Scammon, R. E., and Scott, G. J.: Anat. Rec. **35**:269, 1927.

(2.8 and 1.6 sq. cm., respectively). Thus within three hours of the application of the test the average size of the areas reveals some evidence concerning the degree of group hypersensitiveness to tuberculin, which in individual cases may be obscured by the magnitude of the range of absolute variability. Twenty-four, forty-eight and seventy-two hours following the injection of tuberculin, the tendency noted at three hours is more consistent. At each of these periods the average areas of the Mantoux reactions uniformly were progressively larger for each successive group of ten cases. Later (ninety-six and one

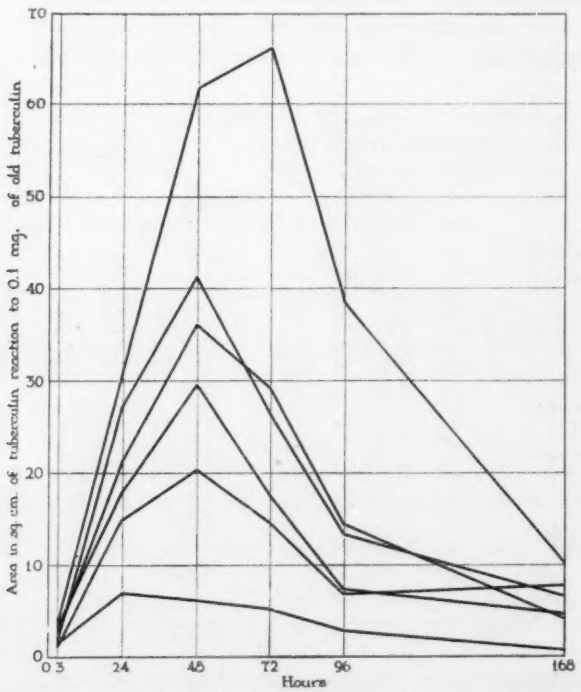


Chart 1.—Curves of growth and area of reaction for groups 1, 2, 3, 4, 5 and 6 (table 2).

hundred and sixty-eight hour readings) as the reactions were subsiding, the averages for the areas of redness also tended to correspond with the relative degrees of allergy manifested by the various groups. In general, therefore, it appears that at corresponding intervals throughout the periods of increment and decline, the area of a positive Mantoux reaction is dependent largely on the degree to which the toxicity of tuberculin in the individual case has been enhanced.

Curves representing graphically the growth and subsequent decrease in the area of tuberculin reactions (chart 1, based on data in table 2) show clearly that in the majority of the cases in which the Mantoux

test was made, the areas of reaction had attained their maximum size forty-eight hours after the injection of tuberculin. The small and very large areas, however, reached full development twenty-four and seventy-two hours, respectively, subsequent to the application of the test. This observation is interpreted as indicating that the time required for an area of reaction to the Mantoux test to reach the maximum size is directly related to the degree to which the individual is hypersensitive to tuberculin. The degree of allergy present also determines the zone in which the curve of growth and decline to the reaction tends to fall.

The average relative rate at which the area of a positive tuberculin reaction grows varies with the period elapsing from the time the test is applied and also with the degree of allergy manifested by the patient. In the majority of cases (table 2), over 60 per cent of the ultimate maximum size of the reaction was attained twenty-four hours after the test was applied, and for the entire group of sixty children the rate of growth during the first day was 1.4 times as rapid as that noted for the second day. The averages recorded in table 2 for the six separate groups, however, show the initial rate of growth to be distinctly more rapid for small than for large reactions. Thus, in general, the observations indicate that the relative rapidity with which the area-growth impulse of the reaction is spent is inversely related to the degree to which a person is hypersensitive to tuberculin. After attaining its maximum development, the subsequent decline in the size of the area of reaction to the Mantoux test, although rapid at first, tended in general to occur at a rate relatively slower than that which prevailed during the preceding period of growth. However, differences in the allergic state apparently do not modify this phase of the reaction in a constant manner.

In this group of sixty children, the maximum area to which the individual tests grew manifested great variability, ranging from 0.33 to 161.29 sq. cm. in size. In the majority of instances (fifty-three cases) the area of reaction did not exceed 60 sq. cm., and for the entire series of sixty children the average maximum area was 32.8 sq. cm. Dickey [3] found a mean area of erythema of about 4.59 sq. cm. (computed from diameters) for seven hundred positive tuberculin reactions in children with various types of tuberculosis. The marked difference in the average degree of allergy present in these two series of cases may have been due to one or many factors, such as the number of cases studied, the type of tuberculosis present, the potency of tuberculin used and the normal variability.

3. Dickey, L. B.: The Size of the Reacting Area in Intracutaneous Tests in Relation to Classification of Disease and to Other Clinical Factors, Am. J. Dis. Child. **38**:1155 (Dec.) 1929.

In my group of children, throughout the phases of growth and decline of the reaction, the areas of redness were observed to vary greatly in extent at each of the different periods for which measurements were recorded. In order to obtain some approximate estimate of the extent of this variability, the coefficient of variation was determined for the set of observations for each period. These coefficients are recorded in table 2, according to which a variability of 112.5 per cent was noted in the area of the reactions three hours after the test was made, which was practically double the variability prevailing at

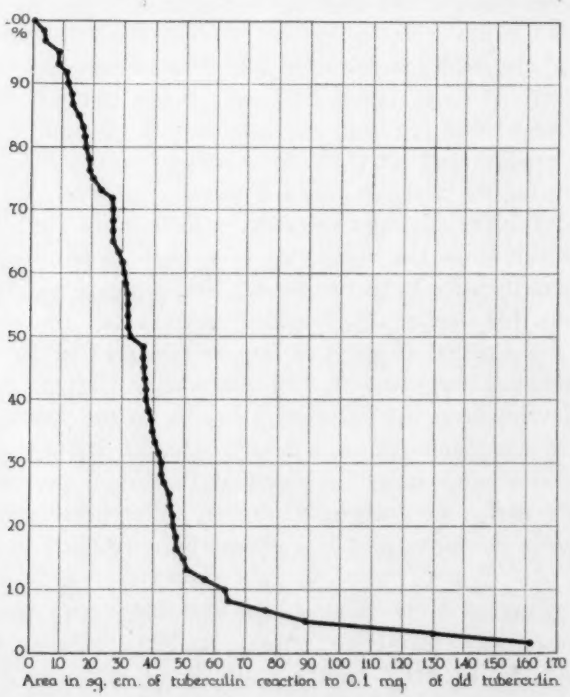


Chart 2.—Cumulative frequency curve cumulating downward, showing distribution of individual cases with respect to the maximum area of reaction to tuberculin.

the twenty-four and forty-eight hour periods (54.1 and 56.7 per cent, respectively). Later (after intervals of seventy-two, ninety-six and one hundred and sixty-eight hours) variability apparently increases again. In general, therefore, when readings are made three, twenty-four, forty-eight, seventy-two, ninety-six and one hundred and sixty-eight hours following the intracutaneous injections of 0.1 mg. of old tuberculin, the areas of positive reaction to the Mantoux test are found to be highly variable at all times, but tend to show the lowest variability at the twenty-four and forty-eight hour periods.

The distribution of the individual cases with respect to the area of the reaction to tuberculin is shown graphically by the cumulative fre-

quency curve (cumulated downward) in chart 2, on which each of the sixty points represents a single observation. By dropping a perpendicular line from any one of the points along this curve and by noting the point at which this line crosses the abscissa, the maximum size that the area of reaction to the tuberculin test attained in that particular person may be readily determined. On this same figure the points of intersection on the curve of horizontal with perpendicular lines reveal the percentage of the group (read on the ordinate) of sixty patients who had areas of reaction to the Mantoux test which were equal to, and greater or smaller than, the area indicated at the point on the abscissa from which the perpendicular lines are erected.

COMMENT

In the series of children selected for this study, primary tuberculous infections experienced in sufficient severity to produce permanent demonstrable calcified intrathoracic lesions elicited abnormal states of allergy which varied tremendously in intensity. To what extent these different degrees of enhancement in the necrotizing tissue toxicity of tuberculin will influence the future welfare of each of these children so far as tuberculosis is concerned is unknown. On the basis of evidence which indicates that allergy is largely responsible for the widespread necrosis of tissue so characteristic of tuberculosis, one may be justified in suspecting that the state of hypersensitiveness to tuberculin present in these children may prove harmful to them later in life if successful reinfections by the tubercle bacillus occur. Reluctance to rely on primary tuberculous infections for protection against the later development of consumption arises when one considers the preceding implications along with certain other unsolved problems. For example, the degree of protective immunity alleged to develop following an infection by Mycobacterium tuberculosis has not been measured, and whether or not it varies in infected persons to the extent that allergy does is unknown. Furthermore, which one of these two (antagonistic?) conditions (allergy and protective immunity) dominates the situation during the balance of the life of the person is debatable.

Lastly, evidence that the immune status of an infected person is definitely superior to the unmeasured but effective power of resistance with which the uninfected body is endowed by nature to combat a primary tuberculous infection fails to be convincing. In spite of these uncertainties, many clinicians are definitely of the opinion that an infection by the tubercle bacillus protects, and consider this phase of the question as closed. Eleven years of follow-up study of tuberculous children at Lymanhurst, which has revealed the development of consumption solely in allergic (tuberculin positive) and never (following infection) in previously nonallergic (uninfected) children, suggests the

advisability of remaining open-minded on the subject. If the experience at Lymanhurst has revealed the truth, then by virtue of the first infection which they survived, these sixty children are now likely to become consumptive should additional intrapulmonary lesions develop later. Further confirmation of this evidence indicating that consumptive persons are mainly (solely?) from tuberculin-hypersensitive groups will force the medical profession to employ methods for the control of tuberculosis similar to those now successfully used by veterinarians, who have proved beyond doubt that certification effectively eradicates and controls bovine tuberculosis. When medical endeavor is raised to the point where it equals veterinary endeavor in this disease, it will no doubt prove to be of inestimable value to mankind. By the institution of methods which guarantee the prevention of tuberculous infection, the need for continued search for the elusive serum, vaccine or other substance which will protect one against this disease will diminish greatly.

SUMMARY

1. A modification of the area-by-weight method suitable for determining the area of the reaction to tuberculin is described.

2. In children who have primary tuberculosis in the calcified and healing stage the area of positive reaction to the Mantoux test attains an appreciable size three hours following an intracutaneous injection of 0.1 mg. of tuberculin.

3. At corresponding intervals throughout the periods of increment and decline the area of a positive reaction to the Mantoux test is dependent to some extent on the degree to which the toxicity of tuberculin has been enhanced in the individual case.

4. The time required for the area of a positive Mantoux reaction to reach its maximum size is directly related to the degree to which the patient is hypersensitive to tuberculin.

5. The relative rapidity with which the area-increment impulse is expended is inversely related to the degree of allergy present.

6. When readings are made three, twenty-four, forty-eight, seventy-two, ninety-six and one hundred and sixty-eight hours following the application of the test, the areas of positive Mantoux reactions are found to be highly variable, but tend to show the lowest variability at the twenty-four and forty-eight hour periods (54.1 and 56.7 per cent, respectively).

7. Certain comments suggesting that a primary tuberculous infection which renders the patient allergic thereafter to tuberculin may be harmful rather than beneficial are offered with the hope that these statements may encourage a receptive attitude toward both sides of the question, pending the final discovery of the truth.

BLOOD CULTURES IN CHILDREN WITH RHEUMATIC FEVER

MAY G. WILSON, M.D.
AND
HELEN EDMOND
NEW YORK

Micro-organisms have been recovered relatively infrequently from the blood of children with rheumatic disease. The majority of bacteriologic investigations have been concerned mainly with the study of cultures from the throat, blood and joints of adults with acute rheumatic polyarthritis.

The recent report of Cecil, Nicholls and Stainsby [1] on the high percentage of positive cultures obtained from patients (mostly adults) suffering from rheumatic fever has stimulated renewed interest in the streptococcic etiology of this disease. Positive blood cultures were also secured in a large number of rheumatic patients by Callow.[2] These investigators emphasized the importance of special bacteriologic technic and ascribed the high percentage of positive cultures obtained in their studies to the methods used.

In view of these recent observations in adults, it was considered of interest to conduct a similar bacteriologic investigation in children presenting the various manifestations of rheumatic disease.[3]

MATERIAL

This investigation covers a two year period—1930 and 1931. Children presenting active and inactive manifestations of rheumatic disease (acute carditis, chorea, arthritis, joint pains, nodules and chronic heart disease) were subjected to one or more blood cultures. As controls, blood cultures were made on: (1) normal new-born infants 10 days of

From the Department of Pediatrics, Cornell University Medical College, and the New York Nursery and Child's Hospital.

1. Cecil, R. L.; Nicholls, E. E., and Stainsby, W. J.: Bacteriology of Blood and Joints in Rheumatic Fever, J. Exper. Med. **50**:617 (Nov.) 1929.

2. Callow, B. R.: Blood Cultures in Rheumatic Fever, Presented November, 1929, Pediatric Staff Conference, New York Nursery and Child's Hospital.

3. Through Dr. W. H. Park, the facilities of the laboratory under the direction of Miss B. R. Callow were afforded us. All of the preliminary studies were made there by one of us (Miss Edmond); thereafter, all mediums and examinations were made in our own laboratory. Miss Callow cooperated with us and assisted us throughout this study.

age and healthy infants and children; (2) children with mild and severe upper respiratory infections, and (3) a miscellaneous group of infants and children who were acutely ill or were convalescing from other infections.

A total of 236 blood cultures from 67 children with rheumatic disease and 153 cultures from 91 subjects of a control group were included for study. In addition, 30 uninoculated blank cultures were subjected to identical examination as a further control.

During the first year (1930), 192 cultures from 58 children with rheumatic disease and 72 cultures from 37 subjects of a control group were studied. The control group comprised 6 healthy children and 9 healthy adults, 8 children and 4 adults with upper respiratory infections and 10 children with various other infections. During the second year (1931), it was considered best to limit the control series to infants and children. A total of 125 blood cultures and 30 uninoculated cultures was included for study. Examination was made of 44 blood cultures of 27 children from the rheumatic series and 81 cultures of 54 children of the control group. The control group comprised 12 healthy newborn infants 10 days of age, 12 healthy infants and children, 10 children with upper respiratory infections and 20 children ill or convalescing from other infections. On identification of the cultures in the 1931 series, it was found that repeated cultures had been taken from 18 of the rheumatic children; therefore, the total number of children for the two years was reduced from 85 to 67.

BACTERIOLOGIC PROCEDURE

The mediums and the routine procedure were similar to those described by Callow,[4] and therefore will be considered only briefly.

Cultures were taken in the outpatient department and on the wards of the New York Nursery and Child's Hospital. The skin was painted with iodine and washed with alcohol; the syringe (10 cc.) and needles were wrapped separately and autoclaved. From 5 to 10 cc. of blood was withdrawn from the median, basilic or jugular veins, and from 3 to 5 cc. of this blood was introduced into each of two 200 cc. bottles, designated A and B. Each bottle contained 100 cc. of double beef infusion broth adjusted to a p_H of 7.8. In order to control the bacteriologic procedure, it was decided to conduct this second study in 1931 as a blindfold test and to include as a further control, a series of uninoculated cultures. All blood cultures and uninoculated cultures were designated by number and subjected to identical bacteriologic examination without further identification. The results were recorded prior to the identification of the cultures. The control blank cultures were opened at the bedside, and the syringes were inserted into the necks of the bottles, but no blood was introduced. All cultures were placed in the incubator, where they remained for four weeks. Subcultures were made weekly.

4. Callow, B. R.: Bacteriologic Investigation of the Blood in Rheumatic Fever: Presenting Evidence of Dissociation of Micro-Organisms Recovered from Blood Cultures, J. Infect. Dis. **52**:279 (May-June) 1933.

For the first three subcultures, 0.5 cc. was pipetted from the original bottle and divided between one tube each of double beef infusion broth and cooked meat beef heart broth, which subcultures were then incubated for three days. For the fourth and last subcultures, 5 cc. of blood broth culture from each original bottle was centrifugated for one-half hour at high speed. The supernatant fluid was poured off and 7 cc. of double beef infusion broth or cooked meat beef heart broth added; the whole was shaken carefully and incubated for three days. The original cultures were then discarded. At each subculture, smears were stained with the Gram stain, and blood agar and ascitic agar plates were streaked. All subcultures were made inside a hood protected from drafts.

RESULTS

A total of 536 blood cultures and 32 uninoculated cultures were sent to the laboratory for study. One hundred and forty-seven (27 per cent) of the blood cultures and 2 of the uninoculated cultures yielded organisms that were considered contaminants and which were discarded. The majority of the contaminations were gross and apparent before the original cultures were opened. With the exception of 10 of the blood cultures and 1 of the uninoculated cultures, the organisms were recovered on the first opening of the bottles. The contamination of these original culture bottles obviously occurred before the cultures reached the laboratory. The remaining contaminations must have occurred during the bacteriologic procedure. The organisms recovered were the usual laboratory contaminants, staphylococci and air-borne bacilli.

The frequency of contamination of the original culture bottles prompted an investigation of the skin as a possible source. The skin was prepared in the routine manner, and 35 sterile needles that merely punctured the skin were cultured. These were each transferred to tubes of broth and observed for a period of three weeks. From 29 per cent of these cultures, staphylococci and air-borne bacilli were secured. It is of interest to note that this is comparable to the 27 per cent contaminations obtained on examination of the blood cultures. That the skin is an obvious source of contaminating organisms is evident from the results obtained from 35 skin swabs that were rubbed on the prepared skin. From 71 per cent of these swab cultures, similar organisms were recovered. In addition, 1 gram-positive diplococcus and 1 diphtheroid were obtained. These results indicate the necessity of more rigid skin preparation in taking routine blood cultures.

The remaining 389 blood cultures were studied over a period of thirty-two days. Two hundred and ninety-three (75 per cent) were sterile and 96 (25 per cent) were considered positive. Of the 32 uninoculated cultures sent for examination, 30 (94 per cent) remained sterile throughout the period of study. Since these cultures were subjected to identical bacteriologic study, the results secured would indicate

that the mediums and bacteriologic method used in this investigation were adequately controlled.

An analysis of the results secured on examination of the blood cultures for the two years indicates that a bacteremia was presumably present in 46 per cent of the children of the rheumatic series (236 cultures from 67 children). It is of interest that 37 per cent of the positive cultures were obtained during the period of rheumatic activity and 41 per cent during an apparently inactive period of the disease.

Similarly, in the entire control group, positive cultures were secured in 41 per cent of the subjects (153 cultures from 91 subjects). In this group 26 per cent of the healthy subjects were found to have positive cultures. If we exclude the 9 healthy adults (in the 1930 series, all of whom had negative cultures), 33 per cent of the healthy infants and

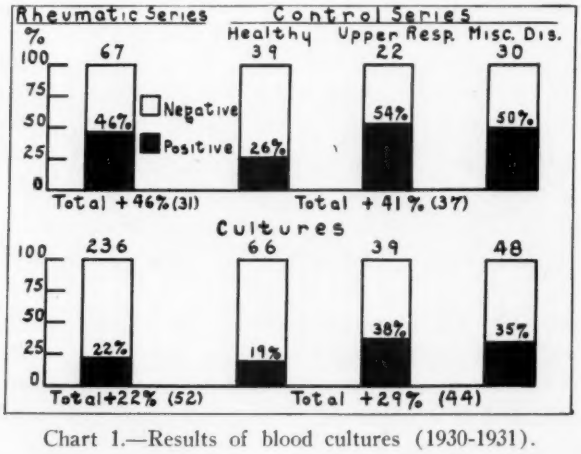


Chart 1.—Results of blood cultures (1930-1931).

children gave positive cultures. Of the remaining subjects in the control group, positive cultures were obtained in 54 per cent of those with upper respiratory infections and in 50 per cent of the children ill or convalescing from other infections (including 4 patients with pneumonia, erysipelas, subacute bacterial endocarditis and sepsis, respectively).

If we compare the actual number of cultures that were positive in each group, it is found that in 46 per cent of the children in the rheumatic series in whom positive cultures were obtained, only 22 per cent of the 236 cultures examined were positive. In the control series, however, 29 per cent of the 153 cultures examined were positive, although only 41 per cent of the patients had positive cultures. A detailed analysis of the results obtained in the 1930 and 1931 series, respectively, is given in the accompanying table.

Results of Blood Cultures

1930 Series

Total no. positive...	Subjects: Rheumatic, 58 40 per Cent		Subjects: Controls, 37 35 per Cent						Cultures: Rheumatic, 192 28 per Cent		Cultures: Controls, 72 22 per Cent							
			Healthy		Upper Respiratory Infection		Miscellaneous Diseases				Healthy		Upper Respiratory Infection		Miscellaneous Diseases		Uninoculated	
	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage
Number	58		15		12		10		192		27		26		19		..	..
Positive	23	40	1	7	7	58	5	50	38	20	1	4	10	38	5	26	..	..
Negative	35	60	14	93	5	42	5	50	154	80	26	96	16	62	14	74	..	..

Blindfold Tests, 1931 Series

Total no. positive...	Rheumatic, 27 44 per Cent		Controls, 54 44 per Cent						Rheumatic, 44 32 per Cent		Controls, 81 35 per Cent							
			Healthy		Upper Respiratory Infection		Miscellaneous Diseases				Healthy		Upper Respiratory Infection		Miscellaneous Diseases		Uninoculated	
	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage
Number	27		24		10		20		44		39		13		29		30	
Positive	12	44	9	37	5	50	10	50	14	32	11	28	5	38	12	41	0	..
Negative	15	56	15	63	5	50	10	50	30	68	28	72	8	62	17	59	30	100

TYPES OF MICRO-ORGANISMS

The organisms that were recovered from the blood cultures were identified as Streptococcus viridans, Streptococcus anhaemolyticus and pleomorphic bacilli. These organisms are identical morphologically and culturally with those secured by Callow.[5]

A brief description of these organisms follows: The strains of Streptococcus viridans included: (1) lanceolate diplostreptococci producing heavy and homogeneous growths in broth and smooth translucent colonies on ascitic agar plates; (2) long-chained streptococci giving unstable growths in broth, and producing coarsely granular colonies with uneven edges and surfaces. All of the strains of Streptococcus viridans caused some discoloration on the surfaces of blood agar plates, the amount of production of methemoglobin varying with the strain.

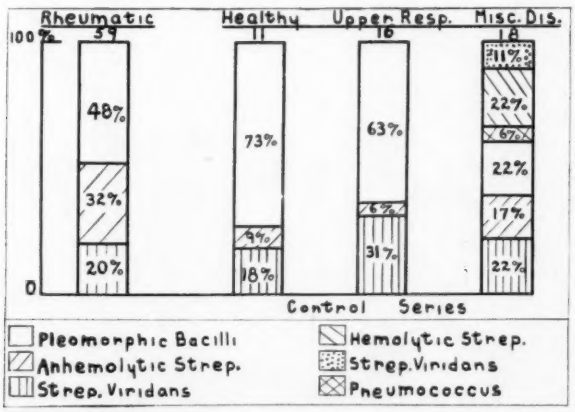


Chart 2.—Type and incidence of organisms recovered from blood cultures.

The strains of Streptococcus anhaemolyticus formed long and short chains and unstable growths in broth, and caused no change on blood plates. All streptococcic strains were bile-insoluble.

All of the strains of pleomorphic bacilli isolated from these blood cultures and included as positive cultures were similar so far as colony studies revealed. Morphologically, they appeared on isolation mostly as oval diplococci which on cultivation developed marked pleomorphism. Some strains were definitely "diphtheroid" in appearance, although this form was also subject to variation. Growths in broth were granular and sparse. The colonies of these organisms were small compared with the larger streptococcic colonies, and on blood agar plates they caused no discoloration. On clear ascitic agar plates, they were seen by trans-

5. Miss Callow confirmed our identification of these organisms. The criteria for identification of these organisms have been described in detail in her investigations.[4]

mitted light to be flat, finely granular throughout and slightly concentrated in the center. A great variation in the size of the several colonies composing a culture was frequently noted.

In the rheumatic series, 20 per cent of the organisms were found to be Streptococcus viridans, 32 per cent Streptococcus anhaemolyticus and 48 per cent pleomorphic bacilli. In the control series, 29 per cent were identified as Streptococcus viridans, 13 per cent as Streptococcus anhaemolyticus and 58 per cent as pleomorphic bacilli. In addition, 2 strains of Streptococcus viridans were recovered from a child with subacute bacterial endocarditis, 4 strains of hemolytic streptococci from an infant with erysipelas and sepsis and a pneumococcus from an infant with pneumonia.

It is evident that streptococci were recovered in about one half of all the cultures in both the rheumatic and the control series, pleomorphic

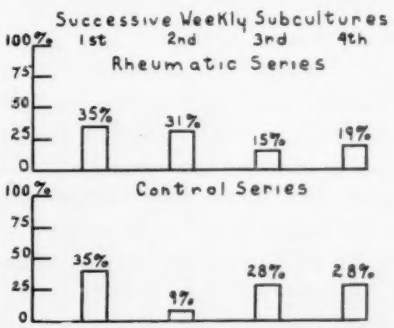


Chart 3.—Percentage incidence of positive cultures.

bacilli being recovered in the remaining half. With the exception of a relatively greater incidence of pleomorphic bacilli in the healthy controls, the distribution of the various strains in the rheumatic and control series was comparable.

The incubation period found necessary for the recovery of these organisms in all the blood cultures, varied from three to thirty-two days. Examinations were made weekly; 35 per cent were recovered on the first subculture, 22 per cent on the second, 20 per cent on the third and 23 per cent on the fourth and final examination. The periods of incubation required for the isolation of streptococci of pleomorphic bacilli were comparable.

Frequently, these organisms were seen on smears, but were exceedingly difficult to grow or did not produce growth. In some instances, organisms were obtained from the original bottle on each subculture. In 7 instances, pleomorphic bacilli were recovered from duplicate cultures of the same specimens of blood. In 4 instances, Streptococcus viridans was recovered from duplicate cultures of the same specimens

of blood. In 3 instances, Streptococcus anhaemolyticus was recovered from duplicate cultures of the same specimen of blood. In 3 instances, pleomorphic bacilli and streptococci were recovered from duplicate cultures of the same specimens of blood. In repeated cultures, negative cultures frequently followed positive ones. In 1 child, 5 positive cultures followed 2 negative ones; in another, 7 repeated cultures were negative.

COMMENT

The assumption that the organisms recovered from the blood cultures of these children had their origin in the blood stream and were not introduced during the bacteriologic procedure would seem justifiable in view of the negative results secured in the uninoculated control series. It is appreciated, however, that it is impossible definitely to eliminate the possibility of contamination with the bacteriologic method used in this study. It is of interest that Callow concluded from extensive control studies that "the organisms described did not originate from the air, skin or sources other than the blood." [4] When we used the bacteriologic technic of this investigator, we recovered identical organisms and were able to secure comparable results.

The streptococci recovered in this investigation are similar to those isolated in numerous studies from blood cultures of patients (mostly adults) with acute rheumatic polyarthritis. Pleomorphic bacilli, however, have been recovered from blood cultures relatively infrequently and are, as a rule, disregarded. It is not within the scope of this investigation to consider their possible significance. However, the trend of recent bacteriologic investigation is toward the recognition of the presence of various forms of micro-organisms due to variation or transformation. Callow concluded from certain transformation experiments "that the bacillary form (pleomorphic bacilli) is one phase and the coccal form (streptococci) another phase in the life cycle of the same organism."

If we assume that the organisms that have been recovered from the blood cultures had their origin in the blood stream of these children, it is obvious that there is no striking difference between the incidence and types of micro-organisms recovered from the blood of the rheumatic and control subjects.

It is worthy of note that in 33 per cent of the healthy infants and children, positive cultures were secured. The occurrence of bacteria in the blood of persons is usually considered indicative of an infection of the blood stream. If we assume that the organisms described had their origin in the blood stream and were not introduced during the bacteriologic procedure, our results would indicate that bacteria may gain access to the blood stream of healthy and of sick infants and children, and are filtered off in various organs where they are destroyed.

We do not know how frequently this may occur or what bacterial species may be concerned. It is probable that, during illness, this transient bacteremia may be increased. It is likewise possible that children may offer less successful barriers to the entrance of bacteria into the blood or that the filter mechanisms are not as adequate. This supposition might explain the negative results obtained by Cecil, Nicholls and Stainsby in their control blood cultures and the small percentage of positive blood cultures obtained by Callow in normal healthy controls. Both of these investigations were for the most part studies of blood cultures of adults. This might also account for the discrepancy in the incidence of the positive cultures in our healthy control series of 1930 and 1931.

Although there are no available data for comparing the incidence of a transient bacteremia in normal and in sick children, it would seem that these results might be considered representative for the bacteriologic procedure used in this study.

In view of the results obtained in the control series, we cannot attribute any specific etiologic significance to the micro-organisms recovered from the blood cultures of children with rheumatic disease. However, it may be possible that the tissues of the rheumatic child are particularly sensitive to the micro-organisms presumably present in their blood stream.

SUMMARY

1. A total of 536 blood cultures were sent to the laboratory for study. One hundred and forty-seven (26 per cent) were found to be contaminated (137 on the first and 10 on subsequent openings) and were therefore discarded. Of 389 blood cultures, 293 (75 per cent) remained sterile for the four week period of study. Ninety-six (25 per cent) of the cultures were considered positive.

2. Thirty-two of the uninoculated cultures were sent to the laboratory (unidentified) and subjected to identical bacteriologic examination. Two, or 6 per cent, were found to be contaminated and were discarded. Ninety-four per cent remained sterile throughout the period of study.

3. Two hundred and thirty-six blood cultures from 67 children with rheumatic disease were studied. In 46 per cent of these children, positive cultures were secured. Positive cultures were obtained in 37 per cent during the active stage and in 41 per cent during an apparently inactive period.

4. In the control series (which included normal infants and children as well as those who were ill or were convalescing from various infections), 153 blood cultures from 78 children and 13 adults were studied. Forty-one per cent of these cultures were positive. Positive cultures were secured in 33 per cent of the healthy infants and children of this control group.

5. The micro-organisms recovered from all of the blood cultures were of 3 types, Streptococcus viridans, Streptococcus anhaemolyticus and pleomorphic bacilli. About one half of the organisms recovered were streptococci; the remainder were pleomorphic bacilli.

6. The incidence of recovery of these organisms from both the rheumatic and the control series was comparable.

7. The incubation period varied from three to thirty-two days. About one half of the strains (streptococci and pleomorphic bacilli) were recovered within a two week period of incubation.

CONCLUSIONS

Organisms may be recovered from the blood cultures of healthy infants and children and from children acutely ill or convalescing from various infections with this bacteriologic method.

In view of the results obtained in the control series, the presence of these organisms in the blood cultures of children with rheumatic disease would not appear to be of primary etiologic significance.

Dr. D. M. Lang, Dr. M. G. Josephi, Dr. V. W. Lippard and the Resident Staff of the New York Nursery and Child's Hospital secured the specimens of blood for us.

1300 York Avenue.

Case Reports

CONGENITAL HEART DISEASE

ATRESIA OF THE TRICUSPID ORIFICE

SAMUEL BELLET, M.D.
AND
HAROLD L. STEWART, M.D.
PHILADELPHIA

Atresia of the tricuspid orifice is an uncommon congenital cardiac lesion. To date only thirteen cases of the true developmental form of this anomaly have been reported. The rarity of its occurrence and the other interesting features presented by this case we believe render it worthy of a report.

REPORT OF CASE

History.—A Negro child, aged 3½ years, was first observed in the pediatric wards of the Philadelphia General Hospital on Feb. 7, 1930. The chief complaints were dyspnea and attacks of choking. The child had had no illnesses of note, aside from occasional colds and two attacks of tonsillitis. She had been short of breath practically since birth, and the parents were told that the child had a "weak heart." However, she was apparently fairly well until the evening prior to admission, when she awoke with an attack of choking, extreme shortness of breath and vomiting. Since that time she had been quite dyspneic, the condition being aggravated when she was in a recumbent posture. Hoarseness was continually present. The family history was unimportant.

Examination.—Physical examination revealed moderate cyanosis and marked dyspnea. There was such respiratory distress that the patient had to be propped up in bed so that she could breathe with any ease. The dyspnea was chiefly inspiratory, and there was inspiratory retraction of the supraclavicular and infraclavicular fossae, the intercostal spaces and the epigastric area during severe attacks. The chest was of the rachitic type. The lungs were clear, except for a few moist râles at the bases. The cardiac impulse was diffuse, forceful and heaving. The apex beat was located in the sixth interspace in the anterior axillary line. A systolic thrill was palpable; it was most marked over the midportion of the heart. A loud systolic murmur was audible over the precordium; it was of greatest intensity at the third left interspace near the sternum. The abdomen was full and protuberant. No masses were palpable. The fingers and toes revealed no evidence of clubbing.

Course.—The child remained comfortable during her stay in the hospital, aside from several attacks of severe dyspnea, which were accompanied by an increase in the cyanosis. She was discharged, somewhat improved, on May 30. On August

From the Division of Cardiology and Pathology, Philadelphia General Hospital, and the Edward B. Robinette Foundation, University of Pennsylvania.

13, she was readmitted with the same complaints, and one week later the tonsils and adenoids were uneventfully removed under ether anesthesia. The patient progressed quite favorably and was allowed to remain in a wheel chair for several hours a day. On November 18, an attack of dyspnea, more severe than any previous one, developed, during which she died.

The temperature had always been within normal limits; the pulse ranged between 100 and 120 (except when the patient was very dyspneic, during which it rose to about 140), and the respirations were about 25 per minute. The roentgen diagnosis was enlarged thymus and congenital disease of the heart. The urine and blood count were normal, and the Wassermann reaction was negative. An electrocardiogram taken on March 4 showed left axis deviation and frequent ventricular extrasystoles. The P waves were notched.

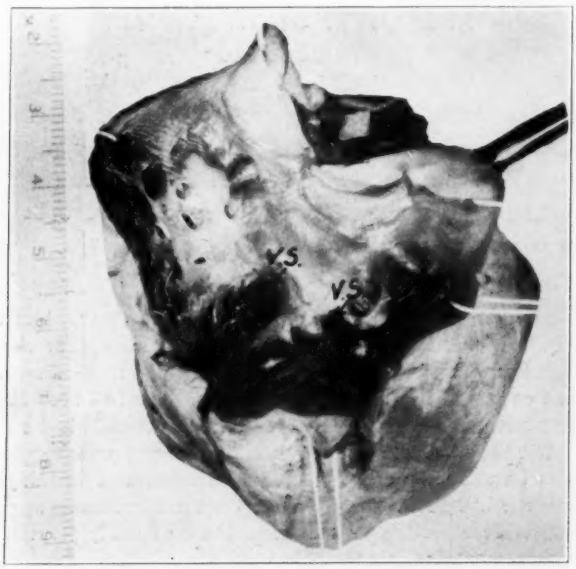


Fig. 1.—Right ventricle. The ventricular walls are drawn back. The patent ventricular septums are indicated by *V.S.* Note the large endocardial crypts. Compare the size of the right ventricle with that of the left in figure 2.

The clinical diagnosis was congenital disease of the heart, probably patent ventricular septum and pulmonary stenosis. Pressure on the recurrent laryngeal by a patent ductus was considered as a possibility in explaining the hoarseness.

Necropsy.—The important observations were limited to the heart which is described in detail. This organ showed marked generalized enlargement. Its weight could not be accurately recorded since it was taken out together with the lungs. The anterior surface was made up practically entirely by the left ventricle. The left chamber was markedly hypertrophied and dilated and constituted practically the entire heart. The left ventricular muscle at its midportion measured 15 mm. and at the apex, 5 mm. Both papillary muscles were hypertrophied, especially the posterior one. The mitral valve was normal. Opening into the right ventricle was a patent interventricular septum. It was elliptic, measuring 6 mm. in the transverse diameter and 4 mm. in the longitudinal. The margin was covered by fibrous tissue.

An accessory interventricular opening, measuring 3 mm. in circumference, was observed below the large opening. The right ventricle was small, being about one fifth the size of the left, and was situated at the upper right corner of the heart as if it were a mere appendage of the left ventricle. There was no evidence of a tricuspid orifice; the blood proceeded directly into the pulmonary artery. Aside from the aforementioned interventricular communication, the ventricular crypts and channels were large, much larger than they usually are even in the adult heart. It is possible that they may have functioned as secondary channels, transmitting blood from the left to the right chamber. The pulmonary artery measured 3 cm. in

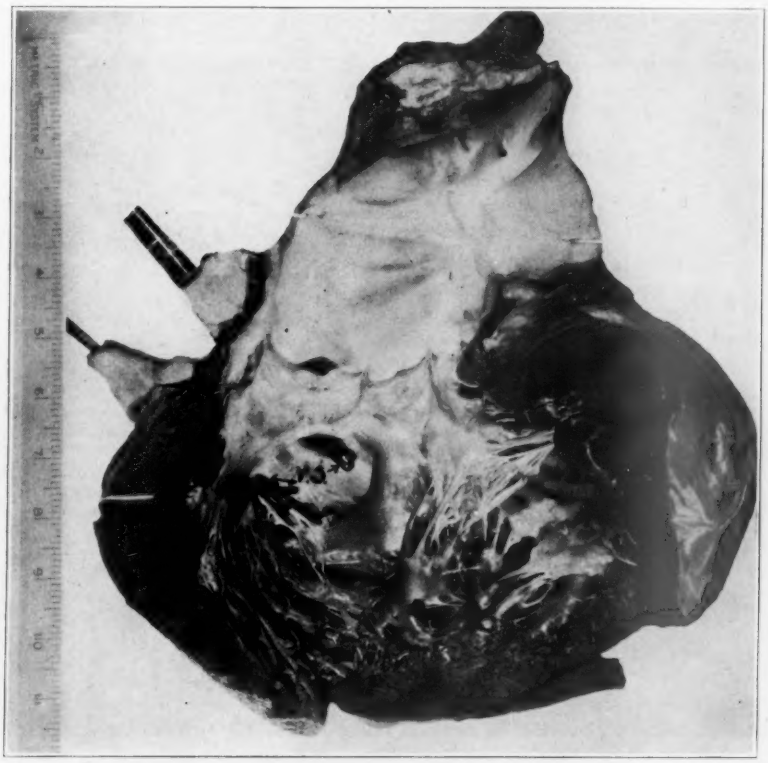


Fig. 2.—Left ventricle. Note the large size of the left ventricle as compared with the right. The probes are placed in the ventricular septums (*V.S.*).

circumference, and its orifice was guarded by three normal cusps. The aorta was considerably enlarged, but otherwise it was normal. It measured 4.3 cm. in circumference. The leaflets were not of uniform size, the posterior leaflet being smaller than the two anterior leaflets. The right auricle was slightly enlarged, and the foramen ovale was widely patent. Separating the right auricular appendage from the right auricle proper were two series of bands, one of which resembled the foramen ovale. The other was perforated by numerous fenestrations. These were probably the remains of the septum between the sinus venosus and the right atrium. The superior and inferior venae cavae entered in their normal position. The right auricle was normal, and the ductus arteriosus was closed.

The pathologic diagnosis was: tricuspid atresia, left ventricular hypertrophy and dilatation, aplasia of the right ventricle, patent interventricular septum and accessory interventricular opening, patent foramen ovale and septum separating the right auricular appendage from the right atrium.

The course of the circulation was as follows: Blood entering the right auricle in the usual manner was transferred to the left auricle through the widely patent foramen ovale. The left ventricle received the blood from the left auricle. From this chamber most of the blood was transmitted to the systemic circulation through the aorta, while the smaller portion was aerated by passing into the right ventricle through the patent interventricular foramina and thence into the lungs through the pulmonary artery. Oxygenation was therefore markedly deficient.

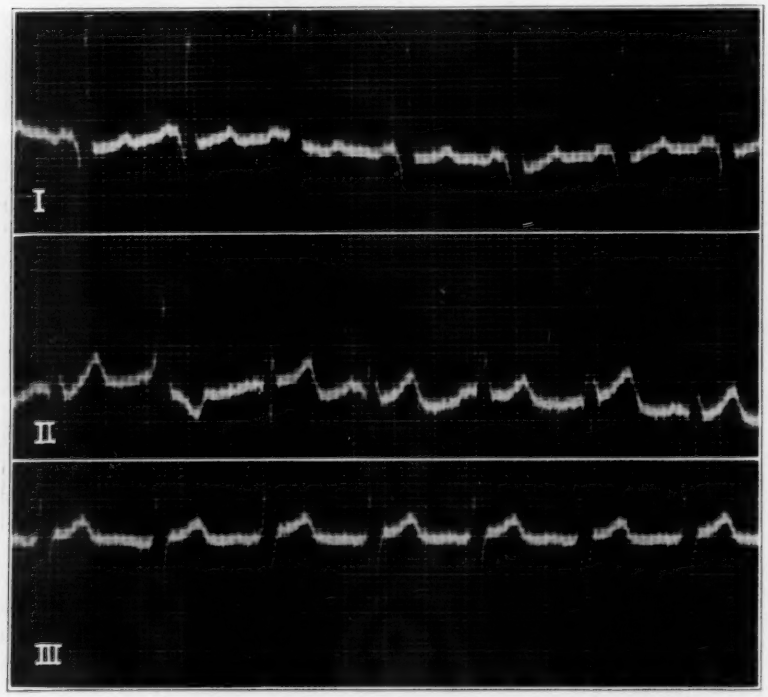


Fig. 3.—Electrocardiogram. Note notching of P wave in leads I and II and the presence of left axis deviation and occasional ventricular extrasystole.

INCIDENCE

From his extensive material on congenital defective hearts Rauchfuss [1] was able to collect but sixteen cases of tricuspid atresia, of which only five cases were of developmental origin. In the remaining eleven cases, the lesion was the result of an inflammatory condition or was of

1. Rauchfuss, C.: Die angeborenen Entwickelungsfehler und die Fötalkrankheiten des Herzens und der grossen Gefässe in Gerhardt: Handbuch der Kinderkrankheiten, Tübingen, H. Laupp, 1878, vol. 4, pt. 1, p. 99.

doubtful etiology. Kühne,[2] in 1906, reviewed the literature of tricuspid atresia and accepted six cases as being of developmental origin. To those she added two of her own. Since then additional cases have been reported by Bernstein[3] in 1906, by Wieland[4] in 1914, by Huebschmann[5] in 1921 (the latter reported two cases of which only the first belongs to this group), by Mönckeberg[6] in 1924, and by Rihl, Terplan and Weiss[7] and Breslich[8] in 1930. Therefore, up to the present time, a total of only thirteen cases of this anomaly have been reported.

THEORIES OF ORIGIN

Rauchfuss[1] has suggested that tricuspid atresia is caused by the overgrowth and fusion of the endocardial cushions, which lead to the obliteration of the tricuspid orifice. Mönckeberg[6] supports the theory of Vierordt[9] that obliteration of the right auriculoventricular orifice results from an unequal division of the primitive atrium by an abnormal shifting of the auricular septum to the right. Abbott[10] stated that in early fetal life the auricular canal opens at first by a common orifice into the left side of the common ventricle and later, by shifting to the right, comes to lie more in the median line. Owing either to the lack or exaggeration of the shifting to the right, a wrong adjustment of the parts would occur, and a mitral or tricuspid atresia would result.

The patency of the interventricular septum is usually explained in the following manner: Since the obliteration of the tricuspid orifice occurs during the fourth week and the interventricular septum does not close until the eighth week of fetal life, it is likely that the mechanical force of the blood flowing from right to left ventricle prevents this

2. Kühne, M.: Ueber zwei Fälle kongenitaler Atresie des Ostium venosum dextrum, Jahrb. f. Kinderh. **63**:235, 1906.

3. Bernstein, E. P.: Case of Congenital Heart Disease, Proc. New York Path. Soc., 1906, p. 29.

4. Wieland, E.: Zur Klinik und Morphologie der angeborenen Tricuspidalatresie, Jahrb. f. Kinderh. **79**:320, 1914.

5. Huebschmann, P.: Zwei Fälle von seltener Herzmissbildung, Verhandl. d. deutsch. path. Gesellsch. **18**:174, 1921.

6. Mönckeberg, J. G.: Die Missbildungen des Herzens, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, J. Springer, 1924, vol. 2, p. 1.

7. Rihl, .; Terplan, K., and Weiss, F.: Ueber einen Fall von Agenesie der Trikuspidalklappe, Med. Klin. **25**:1543, 1929.

8. Breslich, P. J.: Congenital Atresia of the Tricuspid Orifice, Arch. Path. **10**:206 (Aug.) 1930.

9. Vierordt, H.: Primäre Fehler am Ostium venosum dextrum, in Nothnagel, C. W. H.: Specielle Pathologie und Therapie, Vienna, 1901, vol. 15, pt. 2, p. 197.

10. Abbott, M.: Congenital Heart Disease, in Osler and McCrae: Modern Medicine, Philadelphia, Lea & Febiger, 1927, vol. 4.

opening from closing entirely. The presence of the accessory interventricular foramen in our case is very interesting. Its occurrence is probably rare. It is probable that this arose in the same manner as the main interventricular opening, owing to a high intraventricular pressure together with some weakness of the septal wall sufficient to establish and to maintain this opening. The presence of the larger crypts, which probably also aided in the transference of blood from the two ventricular chambers, is also to be explained on a similar basis.

PROGNOSIS

Most of the patients with developmental tricuspid atresia do not live for more than a year. Bernstein's [3] patient lived two years and eight months. This relatively high duration in his case is explained by the almost complete absence of the interventricular septum. The remaining patients of this series lived for relatively short periods of time, from eight weeks to nine months. Our patient lived to be 4 years of age, which is longer than in any of the previously reported cases of this group. The older age attained by our patient may possibly be explained by the accessory interventricular foramen and the large ventricular crypts. When transposition of the great trunks is associated, the circulation is greatly facilitated and life may be maintained for long periods. This is shown by the duration of life in Hedinger's [11] case, in which the patient lived to be 56 years of age.

CONCLUSIONS

A case of congenital heart disease is reported presenting the following anomalies: tricuspid atresia, left ventricular hypertrophy and dilatation, aplasia of right ventricle, patent interventricular septum and accessory interventricular opening, patent foramen ovale and a septum separating the right auricular appendage from the right atrium. The patient lived until 4 years of age, which is longer than did the patients in any other previously reported case presenting this same anomaly. The mechanism of production of this anomaly and its incidence are discussed.

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11. Hedinger, E.: Transposition der grosse Gefässe bei rudimentären linker Herzkammer bei ein 56 jährigen Frau, Centralbl. f. allg. Path. u. path. Anat. **26:** 529, 1915.

COARCTATION OF THE AORTA

ANOMALY OF GREAT VESSELS OF NECK AND INTERMITTENT LEAKAGE OF A CEREBRAL ANEURYSM DIAGNOSED DURING LIFE

H. H. LICHTENBERG, M.D.
CHICAGO
AND
H. F. GALLAGHER, M.D.
LOS ANGELES

Although coarctation of the aorta is recognized during life more frequently now than heretofore, it remains a relatively uncommon and interesting condition. Of approximately 250 cases of the adult type, reported in the literature, only about 25 have been diagnosed during life and confirmed at autopsy. In about 50 others the diagnosis has been made on more or less substantial ground during life. There are, no doubt, many cases that are unrecognized or are unexpectedly discovered at postmortem examination. The reason for this may be that, while the clinical picture is often unmistakable because of the mildness and paucity of symptoms, the physician is often not consulted until a serious complication arises and the condition of the patient makes a careful examination not feasible.

The report of a single case by us seems justified for three reasons: The physical findings are classic; there is an interesting and unusual anomaly of the great vessels of the neck associated with the primary condition, and the patient has survived a serious, usually fatal, intracranial complication. A comprehensive review of the subject of coarctation of the aorta and an admirable statistical study of the condition has been presented by Abbott.[1] Appended to King's [2] paper is a bibliography of the literature to date. The subject has again been more recently reviewed by Blackford.[3] We shall make no attempt, then, to review the literature, save that which is pertinent to the present case.

From the Children's Memorial Hospital and the Otho S. A. Sprague Memorial Institute, Chicago.

1 (*a*). Abbott, M. E.: Blumer's Bedside Diagnosis, Philadelphia, W. B. Saunders Company, 1928. (*b*). Coarctation of the Aorta of the Adult Type, II. A Statistical Study and Historical Retrospect of 200 Recorded Cases with Autopsy, of Stenosis or Obliteration of the Descending Arch in Subjects Above the Age of Two Years, Am. Heart J. **3**:574, 1928.

2. King, J. T., Jr.: Stenosis of the Isthmus (Coarctation) of the Aorta and Its Diagnosis During Life, Arch. Int. Med. **38**:69 (May) 1926.

3. Blackford, L. M.: Coarctation of the Aorta, Arch. Int. Med. **41**:702 (May) 1928.

REPORT OF A CASE

History.—E. L., a white girl, 12 years of age, was admitted on Oct. 28, 1930, to the Children's Memorial Hospital. The family history was unimportant. The patient was born prematurely at the end of seven months' gestation, but she developed quite normally. She had had measles at 2 years, pneumonia at 3 years and mumps six months prior to admission to the hospital. Since her recovery from pneumonia, her father had noticed marked pulsations in the neck. These pulsations were aggravated by exercise, but in general they remained unchanged during the subsequent eight years.

The child had been apparently well until two months before admission to the hospital, when, while playing about the school yard, she suddenly became dizzy and was carried into the school room and placed on a chair, from which she fell to the floor. She remembers only vaguely being picked up and hearing voices about her. Vomiting occurred twice in the next fifteen minutes. The details of the school yard incident are rather indefinite, neither parent having been present, and we cannot be certain whether there were any convulsive movements. When the patient was brought home, she had a high fever; she vomited several times more and experienced extreme dizziness when she turned her head to either side. During the first week of the illness, she refused all food and vomited if urged to eat. The temperature remained elevated for two weeks, and then it gradually subsided. From the onset, the patient experienced a marked weakness of the left arm and leg. When she was allowed out of bed at the end of four weeks, she dragged her left foot and had extreme weakness of the left arm and hand. Her appetite, however, improved, and she felt well again for the next two weeks, except for occasional dizzy spells.

At this time, following a large meal, she again suddenly became dizzy and fell to the floor, and was found unconscious with her eyes rolled upward and both arms extended and twitching. This spell lasted for three or four minutes. The child was put to bed, and by the next morning she felt quite well again.

Since this convulsive seizure, she had been out of bed and felt well except for frequent mild dizzy spells, in which everything turned black before her. Although she remained conscious and could hear people about her talking during these attacks, she found it difficult to respond. She complained also of frequent frontal headaches that were especially severe when she was up and working and that were decidedly relieved by lying down. No pain, tinnitus or sensation of throbbing or pounding had been felt in the head or neck.

Physical Examination.—On admission to the hospital, the child was found to be only fairly well developed and nourished. She had a typical hemiplegic gait, dragging the left foot and holding the left arm close to the body, with the elbow and wrist flexed on the chest. She hopped about easily on the right foot, but was unable to do so on the left. The left arm and hand were decidedly weak. There were marked ataxia and adiadokokinesis of the left side. The deep reflexes were increased on this side. Sensation was normal throughout.

There was a prominent pulsating vessel 1.5 cm. in diameter, extending across the neck about 2 cm. above the suprasternal notch (fig. 1). At the border of the right sternomastoid muscle, this vessel gave off a large branch that could be palpated extending upward beneath the muscle (fig. 2). No pulsations were felt in the suprasternal notch. The heart extended 1.5 cm. outside the left mammary line in the fifth interspace. Its action was regular and forceful, with about 70 beats per minute. The first sound was almost completely replaced by a loud, rough, systolic murmur heard best at the aortic area and transmitted to the entire

precordium and to the vessels of the neck and back, especially to the left interscapular area. The second aortic sound was definitely accentuated. The radial

Fig. 1.—Photograph of patient showing prominent vessel crossing the neck about 2 cm. above the sternal notch.

Fig. 2.—Photograph showing size and direction of anomalous vessel in the neck and its branch running beneath the sternomastoid muscle.

pulsations were regular, forceful and of good volume, but no pulsations could be felt in the abdominal aorta, in spite of a thin, relaxed abdominal wall, or in the femoral, popliteal or dorsal pedal arteries of either leg. On the other hand, abnormally prominent pulsations were present in the neck, axillae and upper inter-

costal spaces and along the borders of the scapulae. An artery, about the size of a lead pencil, lying just beneath the skin, could be felt down the middle of each axilla. The blood pressure on the patient's admission to the hospital was 210 systolic and 170 diastolic in both arms, but it could not be obtained in either leg. Examination of the fundi revealed normal disks, marked pulsations of both the retinal arteries and veins and a small retinal hemorrhage.

Laboratory and Roentgen Observations.—The urine was normal on repeated examinations. The specific gravity varied from 1.009 to 1.021 with the Mosenthal test, and there was 90 per cent excretion of phenolsulphonphthalein in two hours. Chemical examination of the blood gave normal results. The Wassermann tests of the blood and the intradermal tuberculin tests yielded negative results. The

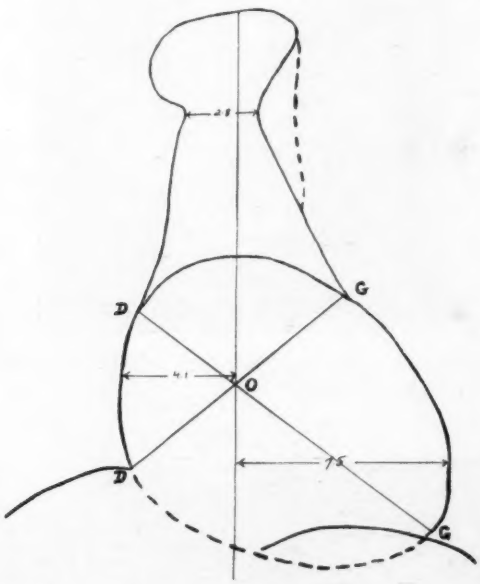

Fig. 3.—Diagram showing the cardiac measurements as follows: weight, 32 Kg. = cardiac area, 10.88 sq. cm.; height, 147 cm. = cardiac area, 64.09 sq. cm.; normal cardiac area, 74.97 sq. cm.; measured cardiac area, 87.00 sq. cm.; measured cardiac area less 5 per cent because of film tracing = 82.65 sq. cm. 82.65 less 74.97 = 8.68 sq. cm., or 10 per cent oversize, $\frac{\text{D. O.} = 4.5 \text{ cm.}}{\text{O. G.} = 8.9 \text{ cm.}}$; index = 0.50; arch = 2.8 cm., and T. D. = 11.6 cm.

spinal fluid was not examined. The electrocardiographic tracings were negative, except for a moderate degree of left-sided preponderance. The x-ray films of the chest, taken at a distance of 6 feet (182 cm.), seemed to show a slight increase in the size of the cardiac shadow. This was not corroborated, however, by actual measurements with the planometer,[4] which showed an increase of only about 10

4. Hodges, P. C.: A Comparison of the Teleoroentgenogram with the Orthodiagram, Am. J. Roentgenol. **11**:466 (May) 1924. Hodges, P. C., and Eyster, J. A. E.: Estimation of Cardiac Area in Man, ibid. **12**:252 (Sept.) 1924.

per cent for the height and weight of the patient (fig. 3). An erosion of a number of ribs could be seen in these films (figs. 4 and 5). Neither in the x-ray films nor with the aid of the fluoroscope were we at any time able to visualize either the entire aortic arch or the large vessel in the neck.

The patient was kept in bed for a few days, during which the blood pressure dropped to 170 systolic and 100 diastolic in both arms. After being observed in the hospital for a number of weeks, the child was discharged to the outpatient department.

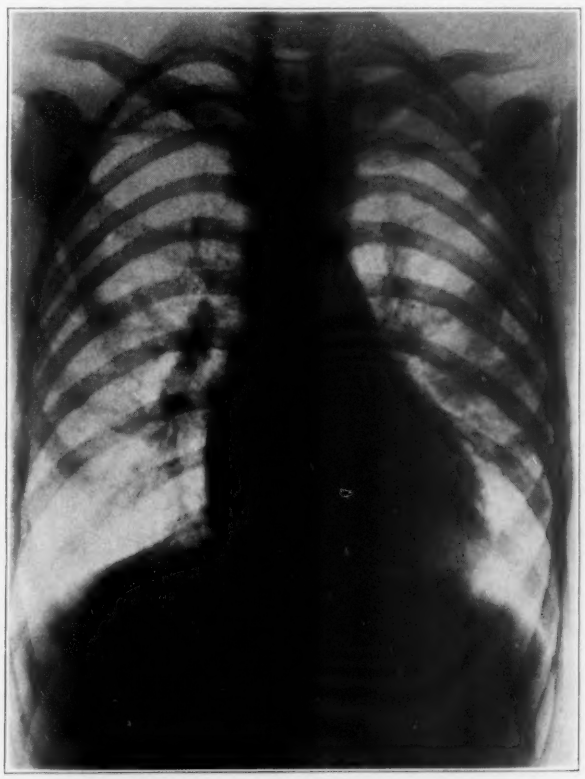

Fig. 4.—Roentgenogram of the chest showing erosions of the fourth, fifth, sixth and eighth ribs on the left and of the second, fourth and fifth ribs on the right side.

Course.—On the visit of Nov. 29, 1930, one month later, the patient complained of tiring easily on walking far and of being able to use the left hand but little. On this examination, the condition was essentially unchanged, except that the spastic paralysis was somewhat more marked. The patient walked with a marked left-sided limp and held the left arm in the typical spastic position. She was seen frequently in the next year, during which the paralysis became less evident, and

she learned to use the left arm fairly well. However, one and one-half years after the onset of the condition, she still lifted the left leg higher than the right and tended to slap the foot down in walking. She presented a picture not unlike that of an arteriosclerotic person who had partially recovered from an intracranial hemorrhage with resultant hemiplegia. The left knee reflex remained hyperactive, and weakness and relative insecurity of the left leg was accentuated in hopping. The left arm was still held slightly flexed, adducted and internally rotated, and did

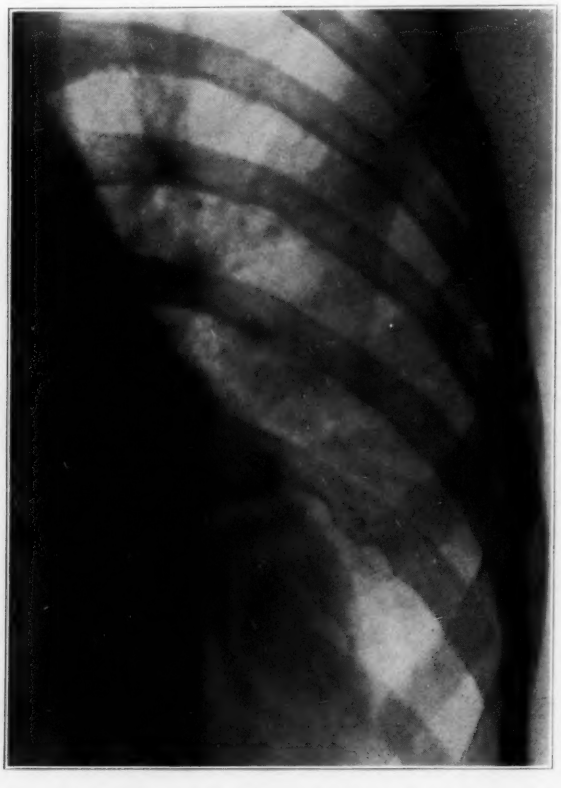

Fig. 5.—Roentgenographic enlargement of the fourth and sixth ribs on the left, to show the erosions in better detail.

not swing as freely as the right in walking. A fairly marked adiodokokinesis could always be elicited.

The patient suffered from repeated moderately severe epistaxes, headaches and dizziness, especially when she was active and bending over. The blood pressure remained about 160 systolic and 90 diastolic in the arms, and was never obtained in the legs. The general condition was satisfactory. The child was gaining weight steadily and attending school regularly. Against our advice, the tonsils and adenoids were removed at another clinic, with however, no unfavorable reaction.

COMMENT

In the presence of the three cardinal symptoms: (1) hypertension in the arms with the blood pressure in the lower extremities unattainable, (2) absent pulsations of the abdominal aorta and arteries of the legs and (3) an extensive collateral circulation manifested by forcibly pulsating, dilated arteries in the neck and thorax, the presence of a rather severe grade of coarctation of the aorta in our patient can hardly be questioned. This diagnosis was confirmed further by the roentgenograms, which showed a marked "scalloping" in a number of ribs, due to the corroding action of the enlarged and tortuous intercostal arteries (fig. 2). This roentgen finding was first described in 1929 by Railsback and Dock,[5] and again by Fray,[6] although it had been recognized in the gross necropsy specimen as early as 1827 by Meckel.[5] Similar lesions may be seen in the x-ray films of Hamilton and Abbott's [7] report in 1928. These authors, however, made no mention of this finding. Neither in the x-ray films nor by fluoroscopic examinations were we able to visualize the entire aortic arch. Fray considers this of diagnostic significance in coarctation.

While neurologic complications are not infrequent, the majority are mild and relatively unimportant, presenting only such symptoms as headache, vertigo, tinnitus, dizziness and rapid fatigue. Intracranial hemorrhage accounts for about 10 per cent of the deaths in coarctation of the aorta. Of the 32 cases with neurologic complications in which necropsy was performed reviewed by Woltman and Shelden,[8] hemorrhage in the brain was found in 37.5 per cent, softening in 19 per cent, rupture of an aneurysm in 9.4 per cent and embolism in 6.2 per cent. Abbott [1b] collected the reports of twenty cases of cerebral hemorrhage due to this condition in 1928. Parker's [9] case is not included in her table, although she makes reference to his paper. Another case not reported is mentioned by Bagley in the discussion of Woltman and Shelden's [8] report, and a twenty-third case is described by Green.[10] Of these, the brain was examined in twenty cases, and spontaneous hemorrhage was

5. Railsback, O. C., and Dock, W.: Erosion of the Ribs Due to Stenosis of the Isthmus (Coarctation) of the Aorta, Radiology **12**:58, 1929.

6. Fray, W. W.: Roentgenologic Diagnosis of Coarctation of the Aorta (Adult Type), Am. J. Roentgenol. **34**:349 (Oct.) 1930.

7. Hamilton, W. F., and Abbott, M. E.: Coarctation of the Aorta of the Adult Type, Am. Heart J. **3**:381 (April) 1928.

8. Woltman, H. W., and Shelden, W. D.: Neurologic Complications Associated with Congenital Stenosis of the Isthmus of the Aorta, Arch. Neurol. & Psychiat. **17**:303 (March) 1927.

9. Parker, H. L.: Aneurysms of the Cerebral Vessels, Arch. Neurol. & Psychiat. **16**:728 (Dec.) 1926.

10. Green, F. H. K.: Congenital aneurysm of the Cerebral Arteries, Quart. J. Med. **21**:419, 1928.

reported in each. Eight patients were found to have aneurysms of the cerebral arteries, with rupture in seven. Abbott [1b] believes that this figure is much too low. She said:

> In view of the extreme difficulty and sometimes impossibility of locating these very small, almost miliary aneurysms on the cerebral vessels in the midst of a large hemorrhage at the base and the extreme youth of most of the patients so dying in this series, it seems safe to conclude the presence of a ruptured cerebral aneurysm in practically all cases of so-called spontaneous cerebral hemorrhage occurring in coarctation before the end of the second decade, without a history of infection or other apparent cause.

That aneurysms of cerebral vessels are present in persons without other anomalies, and that they are not due to hypertension alone, but depend on a congenital defect, was first suggested by Eppinger [11] in 1887. He believed that there was a definite group of aneurysms of the cerebral arteries, especially the small ones, such as those forming the circle of Willis, which depend on a congenital defect and a subsequent tear or dehiscence of the elastica. Since then many observers have come to the same conclusions and have found the cerebral aneurysms, not depending on infection, always at the angles of bifurcation of the vessels.

Further light has been thrown on the subject by the recent paper by Forbus.[12] He studied cases of ruptured cerebral aneurysms occurring in young people, and found, as did Green, that there was an absence of the muscularis in these formations. He demonstrated further that in a high percentage of normal persons there occurs a similar defect of the muscularis at the angle of bifurcation of the cerebral vessels. Vessels in other places, such as the coronary and mesenteric arteries, may possess the same abnormality. Forbus has been able to show that this peculiarity in structure dates from embryonic life, and he believes that it is a relatively normal arrangement. By means of an ingenious experiment, he has indicated that the moving column of blood exerts a greater pressure on the arterial wall at the angles of bifurcation than elsewhere. Since in coarctation there is a constant sustained hypertension in the vessels of the head from early life, it is not surprising to find aneurysms of the cerebral vessels so frequently and intracranial hemorrhage in a relatively high percentage of the cases.

More interesting than the complete rupture of an aneurysm of a cerebral artery, with death from a rapid, widespread hemorrhage, are the cases of "intermittent leakage" of an aneurysmal sac described by

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11. Eppinger, Hans: Pathogenesis (Histogenesis und Aetiologie) der aneurysmen einschliesslich des Aneurysma equi verminosum, Arch. f. klin. Chir. (Supp.-Hft.) **35**:1, 1887.

12. Forbus, W. D.: On the Origin of Miliary Aneurysms of the Superficial Cerebral Arteries, Bull. Johns Hopkins Hosp. **47**:239 (March) 1930.

Parker.[9] In these cases there are periods of disturbed function, alternating with periods of relatively good health. The onset is sudden, with sensation of headache or "a giving away inside the head," and often follows exertion. Fearnsides [13] found this symptom in thirteen of thirty-one cases of cerebral aneurysms of nonembolic origin. The characteristic feature is . . .

> an account in the history of the patient's manifestation of a sudden exacerbation, with apoplectiform onset of symptoms and signs, followed by a period of varying but often considerable (one case went 20 years) duration, in which no fresh developments appeared, followed later by a second or third, or even fourth seizure, in the last of which death from respiratory and medullary pressure occurred, and correlated with this finding at autopsy of evidence of leakage of different ages due to partial ruptures of the aneurysmal sac.

An unruptured aneurysm rarely gives rise to symptoms. Parker believes that it is only in cases of aneurysms with intermittent leakage and focal compression that the correct diagnosis and localization of the aneurysm are possible.

It seems likely that our patient, who has had at least two definite seizures, belongs in this class. Because of the hemiparesis of the left side and periods of difficulty in speech, we believe that the leakage has been taking place in the right rolandic (possibly Broca's) area. It would seem no more surprising to find recovery *quod ad vitam* from an intracranial hemorrhage in a case of coarctation of the aorta than after one due to cerebral arteriosclerosis. Still in none of the cases collected by Abbott nor in those reviewed by us was there a report of a recovery following a hemorrhage. However, in Kolisko's [14] case there was a cortical scar, and in Reinitz' [15] there were an old apoplectic cyst and a history of a stroke occurring three years previously, with recovery, which indicate in these cases at least a similar accident at a previous time, the significance of which was not recognized. One could possibly find other cases like them.

One curious and puzzling finding in our patient was the large pulsating vessel crossing the neck between the sternomastoid muscles, running slightly upward from left to right and giving off a large branch at the border of the right sternomastoid. The presence of this anomalous vessel at once suggested to us the diagnosis of a coarctation of the aorta, in association with either a high riding aortic arch or an anomaly of the great vessels of the neck. Had we been able to feel an aortic pulsation in the suprasternal notch, we would have been convinced of the latter possibility. Nevertheless, because of the relatively small size of the

13. Fearnsides, E. G.: Intracranial Aneurysms, Brain **39**:224, 1916.

14. Kolisko, in Dittrich, P.: Handbuch der ärztlichen Sachverständigen, Leipzig, W. Braumüller, 1913, vol. 2, p. 984, quoted by Abbott (footnote 1 *b*).

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vessel and its direction in the neck, it was probably not the aortic arch. We believe that the innominate artery takes origin on the left side, immediately adjacent to or in common with the left common carotid, as in Murray's [16] case, and extends across the neck to divide at the right sternomastoid muscle into the right common carotid and subclavian arteries.

SUMMARY

A case of coarctation of the aorta with classic symptoms and an associated anomaly of the great vessels of the neck is reported.

The patient presented symptoms of an intermittent leakage of a cerebral aneurysm, probably in the right rolandic area, which has not led to a fatal termination during eighteen months' observation. We have found no record in the literature of a similar condition diagnosed during life.

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Case Reports

"DOUBLE APPENDIX" ASSOCIATED WITH OTHER CONGENITAL ANOMALIES

HENRY N. PRATT, M.D.
BOSTON

The following case is presented because it is believed to be the first reported instance of "double appendix" arising as a congenital malformation and unassociated with inflammation. This and other anomalies of the intestinal tract in the patient bear a striking resemblance to the avian alimentary tract. "Double appendix" appears in quotation marks, for the "appendixes" are believed to be the homologs of avian ceca rather than true appendixes. The possibility of two appendixes in one person may have important medicolegal significance.

A summary of the clinical data and a condensation of the pathologic report follow:

REPORT OF CASE

History.—L. A., a white male infant, entered the hospital on July 29, 1931, at the age of 11 hours, because of an imperforate anus. He was born at full term; the delivery was normal. X-ray plates taken with the patient in an inverted position showed no air-filled intestine in the pelvis or near the anus. On this evidence a sigmoidostomy was performed, with immediate evacuation of a considerable amount of meconium.

Course.—After operation, the patient ran a septic type of temperature. Irrigations were continued through the Mixter tube, and bowel movements were normal in number by this route. The patient went gradually downhill and died on August 13, fifteen days after entry.

The urine contained from 2 to 3 white cells per high power field.

The clinical diagnosis was imperforate anus.

Autopsy.—This was performed at the Children's Hospital on August 13, four hours post mortem. There were no restrictions.

Body: The body was that of a well developed and moderately well nourished, white, male infant measuring 52.5 cm. in length. Rigor mortis was moderate in the hands and jaw and was otherwise absent. Postmortem lividity was slight in the dependent portions. There were no skeletal deformities. The lips were cyanotic. The abdomen was flat, and no organs could be palpated. There was a right rectus operative incision measuring 4 cm. in length. There were no sutures or drainage tubes. The wound was wide open, and loops of intestine could be seen beneath it. The edges were indurated and reddened. The anus was imperforate, being represented by a dimple in the skin not more than 0.5 cm. deep. The body was otherwise normal.

Primary Incision: The body was opened by the usual Y-shaped incision.

Peritoneal Cavity: The peritoneal cavity contained no fluid. In the left lower quadrant beneath the incision several loops of bowel and the great omentum were

From the Department of Pathology, Harvard Medical School, and the Pathology Laboratory of the Children's Hospital.

adherent to the anterior surface of the peritoneal cavity by gray, glistening bands. On dissecting away these adhesions, it was found that there was an opening in the sigmoid which was continuous with the operative incision and was moderately adherent around its edges. The visceral peritoneum covering the entire intestinal tract was reddened, but there was no visible exudate on the surface. The mesenteric attachments were of the midline, embryonic type (fig. 1). The rectum was congenitally absent, while the sigmoid ended in a blind pouch at the base of the posterior aspect of the bladder. The sigmoid was represented by one small loop of fused bowel with a continuous lumen. It was in this pouchlike portion that the sigmoidostomy wound was found. The mesentery was attached around the greater curvature of this fused loop. Above this there were about 7 cm. of intestinal tract, presumably colon, stretching upward and somewhat to the right. At this

Fig. 1.—Semidiagrammatic sketch of the abdominal viscera, showing the midline mesentery (*M.L.M*) and the remnant of the cloacal duct (*C.D.*). The right kidney and ureter are omitted.

point there were two "appendixes" on opposite sides of a slight fusiform swelling, presumably the cecum, each having an individual mesenteric attachment to the ileum. Two lateral taeniae on the colon terminated at the bases of the "appendixes" of their respective sides. No taenia could be recognized along the mesenteric attachment (figs. 2 and 3). The ileum was directly continuous and had practically the same caliber as the preceding colon. From here on, the bowel appeared to be normal ileum and jejunum. The mesentery of the sigmoid and that of the colon were exactly in the midline along the anterior surface of the sacrum. The mesentery of the small intestine also arose in the midline and was continuous with that of the colon. A large portion of the mesentery received its origin from the lower border and the head of the pancreas. The duodenum looped under this mesenteric attachment and had normal relationships. The vessels of the mesentery were slightly distended, while the lymph glands were yellowish

pink and of average size. The liver reached 4.5 cm. below the xiphoid and was normal. The cystic and common ducts were patent. The stomach was not displaced. That portion of the great omentum which customarily forms the gastrocolic ligament in this case stretched from the greater curvature of the stomach to the mesentery of the small intestine. The kidneys appeared large through the retroperitoneal tissues, and greatly dilated ureters could be seen on both sides. The bladder was distended with yellowish-gray, cloudy urine. When pressure

Fig. 2.—Enlarged photograph of the cecum and two "appendixes," showing their mesenteric attachments.

was applied to the bladder, urine could be expressed through the penis, and the ureter of the right side was seen to dilate.

Pleural Cavities: These were essentially normal.

Mediastinum: The arch of the aorta displayed one anomalous branch, the left vertebral artery taking its origin between the left common carotid and the left subclavian arteries. The mediastinum was otherwise normal.

Pericardial Cavity: This was essentially normal.

Heart: The foramen ovale was open and measured about 8 mm. in diameter. The ductus arteriosus was also open and had a caliber of about 2 mm. The heart was otherwise normal.

Lungs: The right lung displayed an anomalous lobe, the superior and lateral aspect of the lower lobe having a groove running around it so that there was a small, roughly pyramidal lobe separated from the lower lobe, measuring approximately 2 by 1.5 by 1.5 cm. There were reddening and diminished crepitus in the dependent portions of the right lung and at the hilus of the left.

Spleen: The malpighian corpuscles were not visible. Otherwise, the spleen was normal.

Alimentary Tract: The mucosa was smooth, moist and slightly congested. The two appendixes had lumina continuous with that of the cecum, the lumen of

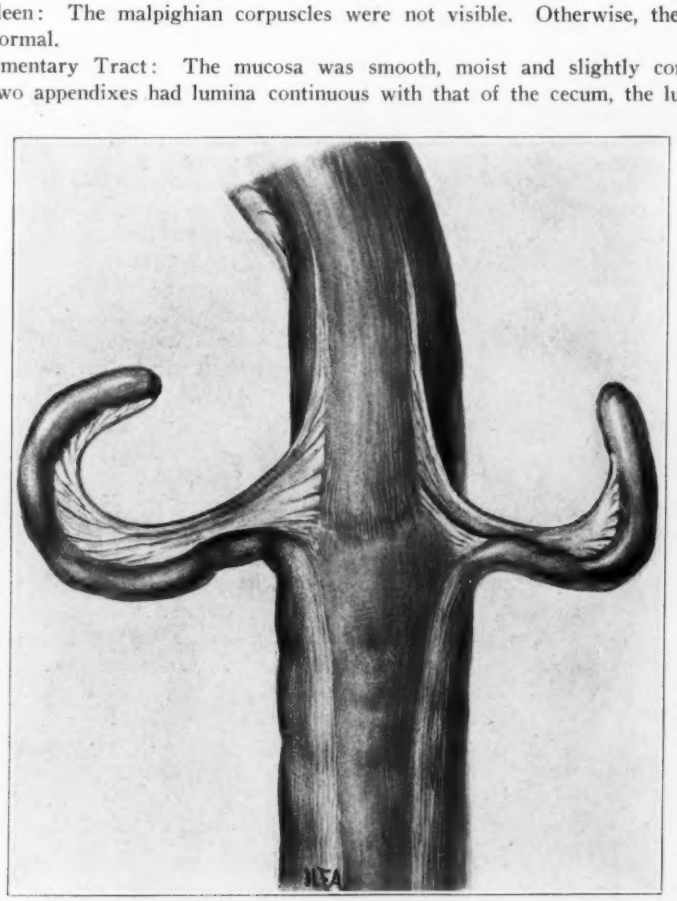

Fig. 3.—Drawing of cecum and two "appendixes," showing their mesenteries and the taeniae of the colon.

the right "appendix" being greater than that of the left. The distal end of the ileum telescoped into the cecum for a distance of approximately 3 mm., thereby forming a roughly circular ileocecal valve. Beneath the curtain formed by this fold the lumina of the two "apendixes" opened. At these points the cleft behind the valve was deeper (fig. 4).

Pancreas: This was essentially normal.

Gallbladder: This organ was essentially normal.

Kidneys: Both kidneys displayed marked fetal lobulations and were very soft in consistency. The capsules were thin and stripped easily. On making coronal sections, from 3 to 4 cc. of grayish-yellow, cloudy urine welled up into the cut.

The pelves and calices on both sides were greatly dilated, so that the cortex, medulla and pyramids were not clearly defined. This was more marked on the right than on the left. The whole width of the parenchyma of the kidney was not over 2 mm. in any portion. The mucosa of the calices and pelves was mildly inflamed. Both ureters were markedly dilated, measuring 16 mm. at their points of greatest circumference, and both had a stricture just before entering the pelves, where the ureter had a circumference of 5 mm. At these points the ureters were kinked, and the mucosa was thrown into valvelike folds. Both ureters, however, easily admitted a probe. The ureteral mucosa was mildly injected.

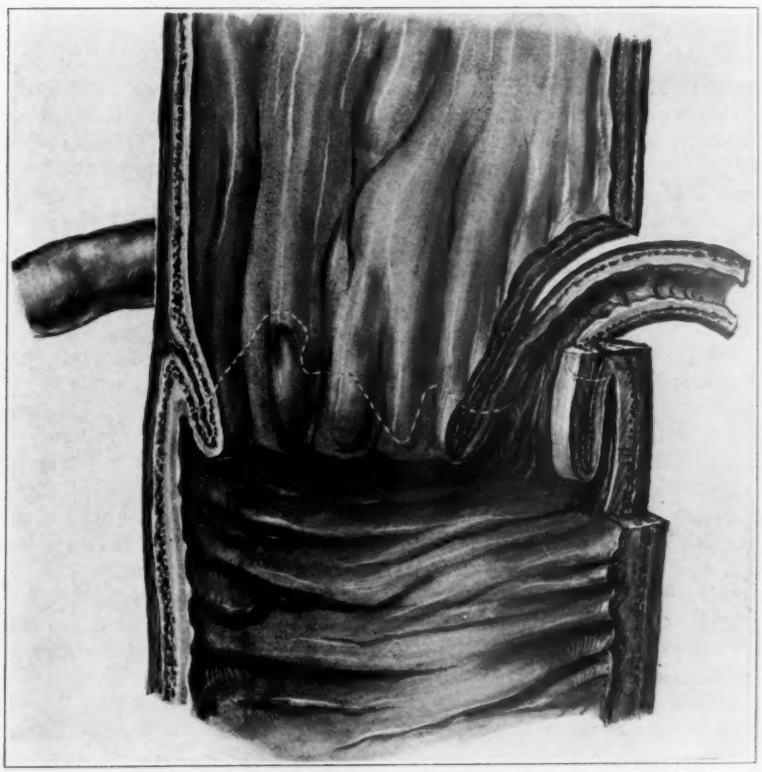

Fig. 4.—Drawing of the ileocecal valve. The cecum has been cut down the anterior midline and laid open. Portions have been cut away to show the opening of the left "appendix" into the cecum beneath the curtain formed by the ileocecal valve.

Suprarenals: These glands were essentially normal.

Pelvic Organs: The wall of the bladder was moderately hypertrophied. The mucosa was markedly injected and contained several hemorrhages. The ureteral orifices were a little more laterally placed than normally, but both were patent, for the probe passed into them with much greater ease than usual. There was insufficiency of the valves, as was shown by the backing up of urine into the ureters by pressure on the bladder. Just above the uvula vesicae a remnant of the cloacal duct was represented by a small dimple which admitted a probe for about 2 mm.

There was no connection between this and the atretic end of the sigmoid. The mucosa in the vicinity of the verumontanum was thickened and thrown into parallel folds. These were not of sufficient prominence to produce obstruction.

Prostate: This was essentially normal.

Penis: The anterior urethra easily admitted a probe and was of uniform caliber throughout. Its mucous surface was mildly injected.

Aorta: This was essentially normal.

Organs of the Neck: These organs were essentially normal.

Thymus: This showed a slight fat replacement.

Thyroid: This gland was essentially normal.

Bone Marrow: This showed active hematopoiesis.

Spinal Cord: This was essentially normal.

Brain: The superior longitudinal sinus was thrombosed along its entire length. The clot in several areas was adherent to the wall of the sinus. The thrombosis involved the straight sinus, the vein of Galen, the internal cerebral veins and the meningeal veins of the cortices on both sides for a distance varying from 1 to 4 cm. Beneath the dura no clots were found, and there was no evidence of inflammation. The pia-arachnoid was moderately congested. The brain was uniformly soft in consistency and quite friable.

Middle Ears: These were essentially normal.

Brain After Fixation: Coronal sections were made approximately 1.5 cm. apart. When the first section was made, blood came freely from both lateral ventricles, more from the right than the left. Anteriorly, the floor of the left lateral ventricle was very soft and necrotic, so that considerable portions of the cortical tissue were involved for a distance of 4 or 5 mm. Around both lateral ventricles throughout their entire length, except in the temporal horns, there were extensive small petechial hemorrhages which lay particularly in the fiber tracts converging from the cortex near the roof of the ventricles. The thalamus, however, was only slightly involved on each side. The internal capsule in its medial aspect on the right was considerably softened, while on the left it was only slightly softened where it lay adjacent to the ventricle. The internal cerebral veins lying on the floor of both lateral ventricles were thrombosed. Both lateral ventricles contained large blood clots in their middle and posterior portions, considerably more on the right than on the left. In the posterior horn of the right lateral ventricle, particularly in its roof, there was a large area of softening which extended into the brain substance for a distance of from 1 to 1.5 cm. The ependymal surfaces were eroded away and were necrotic in the areas of softening. The choroid plexuses were somewhat disguised by the blood clots, but were present in their customary locations. They did not appear abnormally congested in spite of the contiguous hemorrhage and thrombosis. The foramina of Magendie and Luschka were patent.

Microscopic Examination.—Heart: There was mild congestion; otherwise, the heart was normal.

Lungs: There were incomplete expansion, a mild peribronchitis and a mild interstitial pneumonitis.

Spleen: Congestion and a small amount of hematopoiesis were found.

Ileum and Colon: There was mild congestion; otherwise, the ileum and colon were normal.

Ileocecal Valve (fig. 5): Several sections showed the fold of ileum stretching down into the cecum. The mucosa of the upper or ileal end of the fold was thrown

into villi typical of small intestine. This merged into typical large intestinal mucosa, which covered the greater part of the valve. The submucosa of the flap was rich in lymphoid tissue. The tunica muscularis of the valve consisted of two layers of circular muscle fibers separated by a single longitudinal layer, the latter being continuous with the longitudinal muscle bundles of the ileum and cecum and formed by the fusion of the two. The valve itself had no serosa.

"Appendixes": Many cross-sections taken at different levels showed that both appendixes had mucosa like that seen in the large intestine (figs. 6 and 7). The epithelial lining was fairly well preserved. The left "appendix" had a smaller lumen than the right, owing to the greater length of the glands in the former. The blood vessels of the mucosa were mildly congested. There was only a small amount of lymphoid tissue in the submucosa of either "appendix." There were several lymphatics filled with lymphocytes running through the submucosa. There was no inflammatory reaction. There were two muscular layers, an inner longitudinal and an outer circular one. These were of exactly the same thickness in both "appendixes," proving that the smaller lumen of the left one was not due

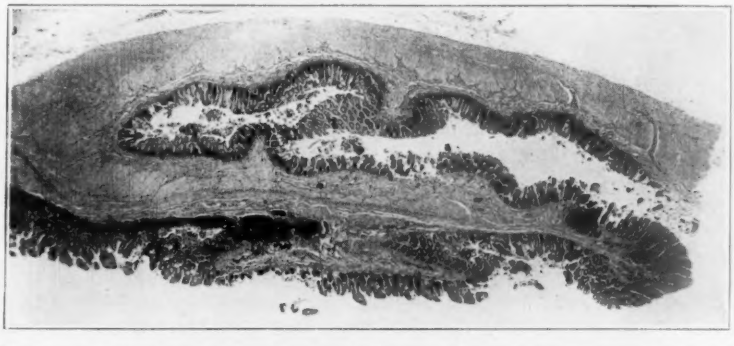

Fig. 5.—Photomicrograph of a longitudinal section of the ileocecal valve, showing the gradation of mucosa from that of small intestine to colon; × 10.

to contraction of the tunica muscularis. The serosa showed no inflammation or thickening.

Liver: There was a mild fat infiltration; otherwise, the liver was normal.

Kidneys: There were pyelonephritis, thrombosis of the larger vessels, many being dilated, and infected collecting tubules with fibrosis of the related glomeruli and convoluted tubules.

Ureter: There were a mild, chronic inflammation of the mucosa and submucosa and hypertrophy of the muscularis.

Bladder: There were hypertrophy of the musculature and a mild chronic inflammation of the mucosa.

Penis: Serial sections failed to show obstruction of the urethra. There was a mild balanitis.

Suprarenals: Slight medullary hemorrhage was present; otherwise, the glands were normal.

Thymus: This showed involution.

Thyroid, Trachea and Esophagus: These were essentially normal.

Pituitary: Mild congestion was present; otherwise, the body was normal.

Umbilical Vein: This was thrombosed.

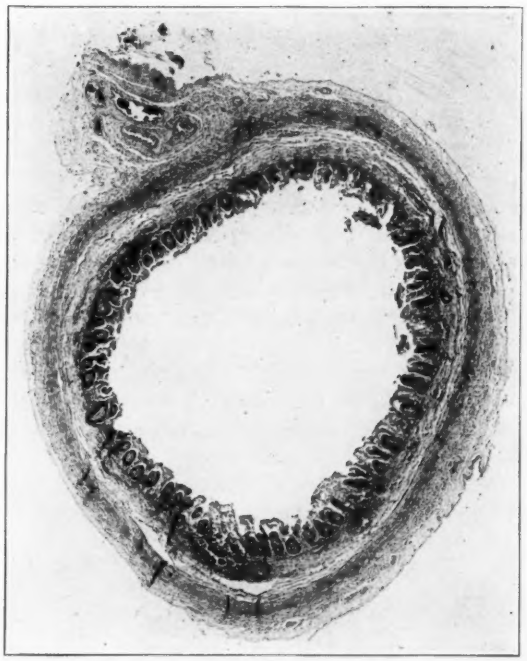

Fig. 6.—Photomicrograph of a cross-section of the right "appendix"; × 46.

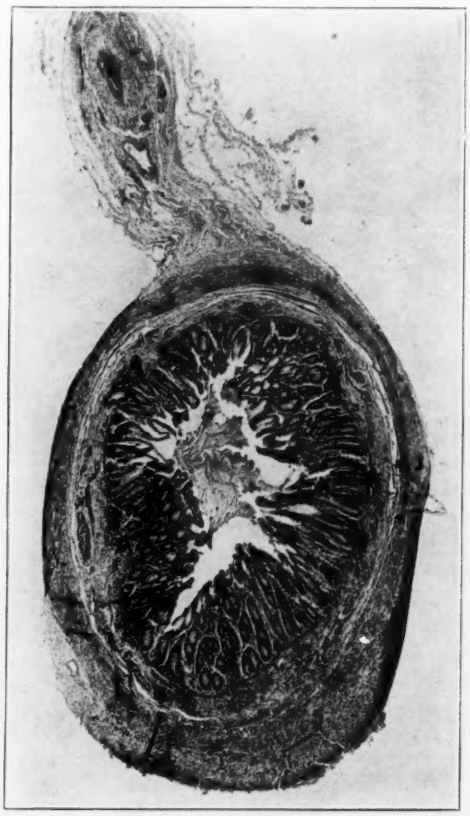

Fig. 7.—Photomicrograph of a cross-section of the left "appendix"; × 46.

Blood Clot from Sagittal Sinus: The thrombus was of antemortem origin, as evidenced by an ingrowth of fibroblasts.

Spinal Cord: This was essentially normal.

Bone Marrow: Active hematopoiesis was present.

Brain: There were petechial hemorrhages, extensive thromboses of the meningeal and cerebral vessels, necrosis and meningitis localized to the areas immediately adjacent to the thromboses. Giemsa stains showed no organisms in the thrombi, vessel walls or meninges.

Pathologic Diagnoses: There were "two appendixes"; imperforate anus; congenital atresia of the rectum; anomalous mesentery; anomalous colon; balanitis (mild); hypertrophy of the bladder; cystitis (mild); persistent cloacal duct; incompetency of the ureterovesicle valves; megalo-ureters (bilateral); ureteritis; congenital anomaly of the kidneys (polycystic); pyelonephritis (bilateral); anomalous lobe of the right lung; anomalous branch of the aorta; thrombosis of the superior sagittal sinus, straight sinus, vein of Galen, internal cerebral vein, meningeal vessels, umbilical vein, renal veins and small vessels of the thyroid and the pituitary body; localized meningitis; hemorrhage into the ventricles of the brain; softening of the brain (periventricular); interstitial pneumonitis; incomplete expansion of the lungs; peribronchitis; congestion of the myocardium, lungs, spleen, gastro-intestinal tract, kidneys, ureters, bladder, penis, thymus, pituitary body, mesenteric glands and brain; fatty infiltration of the liver; petechial hemorrhages in the suprarenal medulla, meninges and brain; involution of the thymus, and right rectus incision.

Postmortem Bacteriology.—Cultures of the peritoneum and heart's blood showed no growth.

REVIEW OF THE LITERATURE

A search of the literature reveals only four cases of double appendix. None of these, however, with the possible exception of one, are true congenital malformations.

Braatz, in 1929, cited the case of a young woman who was operated on for appendicitis. Ten months later the patient came to him with a discharging fistula and abdominal pain. Twice Braatz was assured by the original surgeon that the appendix had been removed. Nevertheless, Braatz determined on a second operation and removed an appendix that was attached at the usual site on the cecum, which gave the histologic picture of appendix. Braatz concluded that the first operator must have left a large stub of the original appendix in the mass of adhesions around the cecum and that it was this stump that was removed at the second operation.

Elwyn reported the case of a 19 year old girl who had symptoms suggesting appendicitis. At operation a forked appendix was removed. The two crura took their origins from the left and right cecal pouches and were fused at their distal ends, having a common lumen for a short distance. Histologic examination revealed normal appendical tissue in both limbs.

Goldschmidt, in 1930, reported an unusual instance of double appendix. The patient had the signs and symptoms of acute appendicitis. These subsided, to flare up again later, at which time a laparotomy

was performed. Two appendixes were found, the first having the usual anatomic relations and the second being very short and applied on the cecal surface. It had a mesentery and contained a fecolith. This small appendix did not have a lumen continuous with that of the cecum, for when it was removed it left only a serosal defect. On microscopic examination it showed exactly the same histologic structure as the normally situated appendix. Neither one presented an acute reaction. Goldschmidt expressed the belief that at the time of the first attack the distal end of the appendix amputated itself and became implanted on the cecum.

In 1931, Walthard reported the finding of double appendix associated with an umbilical fistula. The two appendixes, however, arose from a common base. Embryologically, there appears to have been but one appendix that bent double on itself, with the distal end becoming involved in the fistula.

EMBRYOLOGY AND COMPARATIVE ANATOMY

In the 7.5 mm. human embryo the primitive intestine consists of a single loop that has not yet undergone torsion and has not yet migrated into the umbilical cord. At this time a swelling appears in the lower limb of the primitive loop. This represents what eventually develops into the cecum and vermiform appendix. During torsion of the primitive loop and throughout the migration of the intestine into the umbilical hernia, this swelling continues to grow at the same rate as other portions of the bowel. When the intestine is withdrawn into the celomic cavity and torsion is completed, this cecal swelling comes to lie beneath the liver. The proximal fifth of the cecal swelling continues to grow so that its caliber is the same as that of the contiguous intestine. At 11 weeks the distal four fifths of the cecal swelling shows retardation in growth and finally becomes the vermiform appendix. There is no point in the formation of the human appendix where doubling might logically be expected to take place. A true vermiform appendix is found only in man, the higher apes and the wombat. The little ant-eater is the only mammal possessing two well defined cecal processes or pouches. Some armadillos have bilateral cecal swellings.

In birds, however, two ceca develop, one on either side of the primitive intestinal loop at the point where the single cecum appears in the human embryo. They first manifest themselves as bilateral swellings on the sixth day. They grow rapidly as finger-like processes and attain a considerable length. In some birds, such as the pigeon, the adult ceca are represented by two small tubercles, while in other birds, such as the grouse, the ceca may be a yard long. As a general rule, birds have a short alimentary tract with a fairly uniform diameter so that the

many foreign bodies swallowed with the food may be rapidly expelled. The openings into the ceca are too small to admit pebbles and undigested seeds. In two domestic fowls that I dissected, these openings were guarded by small, valvelike, crescentic folds of mucosa (fig. 8). The ceca contain only alimentary matter. They are regarded as the analogues of the mammalian colon. The ceca probably have digestive and absorptive functions.

Fig. 8.—Drawing of the ileocecal valve of a domestic fowl for comparison with figure 4. The gut has been split longitudinally along the midline and laid open. Note the folds of the mucosa partly occluding the openings of the ceca.

No literature on the histology of the avian alimentary tract could be found. Consequently, sections of the intestines and ceca of the dissected fowl were prepared. As in man, the small intestine could be differentiated from the large by the presence of villi and a relatively small amount of lymphoid tissue. The rudimentary ileocecal valve showed gradation of the mucosa from that of small to large intestine very much like the change noted in the case described. The ceca were lined by large intestine mucosa with approximately the same amount of lymphoid tissue.

COMMENT

In the case reported, Prof. S. B. Wolbach first pointed out that the presence of two "appendixes" was suggestive of avian morphology. The "appendixes" are entirely separate, lie on opposite sides of the intestine and are directed upward, as are the ceca in birds. Each appendix has its individual mesentery attaching along the adjacent ileum. Each lumen is continuous with that of the bowel. The histologic picture of both "appendixes" is essentially alike. The glands of the left "appendix" are longer and deeper than those of the right, thereby giving the former a narrower lumen, but neither can be definitely differentiated from the large intestine or cecum. Since all these structures have essentially the same layers, it is impossible microscopically to distinguish them from each other. As a rule, however, the appendical mucosa has a larger quantity of lymphoid tissue than that of the cecum or large intestine. Comparison with normal infantile appendixes shows that this may not necessarily be true, for generalized lymphoid hyperplasia has not taken place at this early age. From the microscopic point of view, therefore, it is impossible to say whether these two "appendixes" are true appendixes or ceca.

Four other pieces of evidence, however, point to avian structure:

First, there is a primitive midline mesentery. In the chick embryo the original loop of gut does not undergo torsion, and therefore a midline mesentery continuously attached to both the small intestine and that part of the intestine below the ceca is maintained in the adult bird.

Second, the intestinal tract, as in birds, is of nearly uniform caliber throughout. In the sigmoid the large, pouchlike swelling with a continuous lumen is an exception to this statement. However, the fact that the mesentery is attached around the outer edge of this pouch leads one to suppose that it was formed by the fusion of a loop of sigmoid. The arrangement of the muscle fibers tends to corroborate this theory. The lumen of the segment of bowel taking part in the formation of this pouch is approximately equivalent to that of the remaining intestine. Therefore, if one accepts this view of the genesis of the pouch, the exception may be overruled and from the point of view of embryology one may consider the entire intestinal tract as essentially of uniform circumference.

Third, there is a persistent remnant of a cloacal duct. This is represented by a dimple that will admit a probe for about 2 mm. situated in the mucosa at the neck of the bladder just above the uvula vesicae. In the bird, the intestinal tract and urogenital tract both empty into a common cloaca.

Fourth, associated with the imperforate cloacal duct, there is complete absence of the rectum. This point requires more careful consideration. Keibel had in his collection a human embryo of 11.5 mm.

in which "the epithelium of the lower portion of the intestine blocked the lumen at two small places." Such an obstruction in the lower bowel has not been seen in an embryo after the obliteration of the cloacal duct, and so this may serve the function of preventing back flow of wolffian excretion into the intestines. It is possible that the persistence of such an occlusion with invasion by connective tissue results in the ordinary case of atresia recti. In the chick embryo, however, Gasser in Germany and Minot in America have both shown that this growth of the epithelium in the lower portions of the intestine is a normal occurrence. Usually the lower bowel again becomes patent, and the connection with the cloaca is reestablished. This obstruction occurs on the fifth or sixth day, at the time the original cecal swelling is first becoming manifest. If, in the case reported, the development was arrested at this time, as one is led to suppose by the presence of two ceca, it is logical to expect that the connection between the intestine and cloaca would never be reestablished. This is exactly what happened in this case: the intestinal tract ended in a blind pouch immediately behind the bladder and was fused to it.

As previously described, the colon bears lateral taeniae which fade out as they reach the bases of the "appendixes" of their respective sides. They never converge as do those on the normal cecum. No reference to taeniae in birds could be found in the literature, and they were not present in the two domestic fowls that were dissected.

The ileocecal valve in this case, however, is faintly reminiscent of those found in the fowl. In the former the valve consists of a well defined curtain encircling the lumen of the cecum and covering the openings of the "appendixes," while in the latter two small folds of mucosa partially occlude the cecal orifices from above.

These anomalies cannot be entirely explained on the basis of arrested development. The bird is a distinct relative, not an ancestor, of man, so that the human embryo does not pass through an avian stage in the process of development. One can only surmise that unknown forces similar to those governing the direction of growth of the avian intestinal tract were temporarily active in the case reported. The presence of two ceca or "appendixes" and the atretic rectum suggest that these forces were manifested at a time corresponding in man to the fifth or sixth day of embryonic life in the chick, and that development was arrested shortly thereafter.

The extra lobe of the right lung, the anomalous branch of the aorta, the hypertrophied bladder, the megalo-ureters and the hydronephrosis are all anomalies or results of anomalies that are seen comparatively often and will not be discussed here. They are of interest only in confirming the familiar observation that congenital anomalies are frequently multiple.

CONCLUSIONS

1. A case is reported in which unknown embryonic forces and arrested development have given rise to an intestinal tract closely simulating that of a bird.

2. The embryology, comparative anatomy and possible significance are discussed.

3. This is believed to be the first reported case of "double appendix" arising as a congenital malformation.

Prof. Frederic T. Lewis and Dr. Sidney Farber, of Harvard Medical School, gave valuable suggestions, and Mr. H. F. Aitken made the painstaking and accurate drawings.

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Progress in Pediatrics

PERIARTERITIS NODOSA IN INFANCY AND IN CHILDHOOD

REPORT OF TWO CASES WITH NECROPSY OBSERVATIONS; ABSTRACTS OF CASES IN THE LITERATURE

JACOB L. ROTHSTEIN, M.D.
AND
SARA WELT, M.D.
NEW YORK

Periarteritis nodosa, in adults or children, is a comparatively rare disease of great interest to investigators, whether are are internists, surgeons or pathologists, because of the marked difficulty in correctly diagnosing the condition during life, the bizarre symptomatology and the controversy which exists as to the exact etiology of the disease. The symptom complex may resemble many of the more common and generally well known illnesses, and, in not a few instances, it may so closely simulate an acute surgical abdominal condition that operative procedure may be resorted to mistakenly.

Periarteritis nodosa was first described by Kussmaul and Maier in 1866, and has since borne the former investigator's name, particularly in the continental literature. Prior to that, in 1852, Rokitansky reported the finding of innumerable aneurysms in the wall of small arteries over the entire body, except the brain, in a man 23 years old, who had died with the symptoms of dysentery. In 1887, Eppinger examined a piece of mesentery from this patient and, with improved methods of examination, was able to find lesions identical with those described by Kussmaul and Maier. It is of interest to note that, even earlier, 3 cases of multiple aneurysms had been reported—in 1755, Michaelis and Matani each reported a case, whereas in 1810, Pelletan described a case in which 63 aneurysms were found.

The literature has been well summarized by several authors—Schreiber (1904), Lamb (1914) and Ophüls (1923). It may be of interest to compare the number of cases reported during two periods—one dating from the classic description by Kussmaul in 1866 to Schreiber's report in 1904, and the other from 1904 up to the publication of Ophüls' paper in 1923. The former represents an interval of thirty-eight years during which only 15 additional cases were reported (Schreiber), whereas the latter covers an interval only half as long, nineteen years, during which 53 additional cases had been described (Ophüls).

From the Pediatric Service of Dr. Béla Schick, Mount Sinai Hospital.

More recently, Gruber (1926) summarized the literature and found 117 cases. Singer, in 1927, brought the total number of cases up to 130 (really only 125, for Singer included 5 cases of Arkin by "personal communication," whereas the latter were actually published three years later). In the last few years the number of reports has greatly increased, for up to the time of the writing of this report the total number of cases of proved periarteritis nodosa including our own 2 cases is 195. Thus, there have been at least 77 new cases described in the literature since Gruber's publication in 1926—a period of approximately from five to six years. The increase in the number of case

TABLE 1.—*Authors of Cases Reported in the Literature Since Survey by Gruber in 1926* *

Author	Year	No. of Cases	Author	Year	No. of Cases
Gruber (summarized literature).	1926	117	Baló and Nächtnebel	1929	9
Cleland (not on Gruber's list)	1923	1	van Paassen	1929	1
Christeller	1926	4	Gray (second case)	1929	1
Gray	1926	1	Bennett and Levine	1929	2
Franz	1926	4	Feller	1929	1
Harbitz	1926	2	Nordmann and Reuyss	1929	1
Freund	1927	1	Blum	1929	1
Giese	1927	1	Hutinel, Costé and Arnaudet	1930	1
Basch	1927	1	Stepp	1930	1
Singer	1927	2	Carr	1930	1
Kimmelstiel	1927	4	Arkin	1930	5
Marinesco and Draganesco	1927	1	Herlitz	1930	3
Battaglia	1928	2	Macaigne and Nicaud	1930	1
Debré, Leroux, Lelong and Gauthier-Villars	1928	1	Runge and Melzer	1930	1
Strong	1928	1	Kountz	1930	1
Hauser	1928	3	Stengel	1930	1
Weigeldt	1928	2	Lindberg	1931	1
Nauheim	1928	1	Damblé	1931	1
Brocher and Frommel	1928	1	Goldstein	1931	2
Bansi	1928	2	Hinrichs	1931	1
Böck	1929	1	Troutman	1931	1
Silvermann	1929	1	Vance and Graham	1931	1
Goldstein and Wexler	1929	1	Present report	1932	2
Total number of cases					195

* For references, see bibliography.

reports would seem due not to a greater incidence of the disease but rather to a more widespread and thorough knowledge of its characteristics and to a more careful and complete microscopic examination on necropsy. Table 1 represents a list of the proved cases reported in the literature since Gruber's survey in 1926.

The disease is said to be four times as frequent in males as in females. It may occur at any age, the youngest patient reported being 3 months of age; the oldest, 78 years. About half of the cases occur during the third and fourth decades of life. In this paper we are concerned with the cases occurring in children, and we have gathered from the literature a total of 21 cases of periarteritis nodosa occurring in infancy and childhood up to the age limit of 15 years. Including the 2 cases reported here there have been 23 cases in children in a total

of 195 cases of the disease, or a percentage incidence of 11.8 during childhood.

The duration of the disease may vary from a few weeks to six months, rarely one year. In Fishberg's case, symptoms appeared only six days prior to death and in Thinnes' case of a 9 month old infant the illness was apparently of only four hours' duration. Obviously, in both cases the disease must have been present for a longer time without any symptoms having been manifested. Definite periods of remission and exacerbation have been observed, indicating a tendency toward healing. Manges and Baehr reported a case in which the acute periarterial inflammatory process, as evidenced in a mesenteric node removed at laparotomy, had long subsided and the disease had been progressing toward healing when death occurred three months after laparotomy, due to renal insufficiency. Spiro reported a case of similar nature in which all arterial lesions found at autopsy had advanced to the stage of healing. More recently, in Arkin's case of histologically healed periarteritis nodosa the patient lived four years after his one and only attack of acute illness, death taking place from renal and cardiac insufficiency.

Clinically, the syndrome is that of a fairly acute or chronic sepsis with a varied local symptomatology. The general symptoms occurring with most regularity are those commonly associated with infectious disease—irregular fever, increasing weakness, prostration, anemia, tachycardia, often an enlarged spleen and a leukocytosis which may be quite marked. Associated with these more general symptoms, notably those of sepsis, are others due to widely scattered vascular changes within the body. The wide variation in the latter group of symptoms depends almost entirely on the difference in the location of the pathologic process. To illustrate, "rheumatic" pains are the result of the myositis due to the closure of diseased muscle arteries; albuminuria and hematuria may be evidences of renal infarction, whereas signs of renal insufficiency may be the result of atrophy of the tubules and fibrosis secondary to involvement of renal arteries; intestinal hemorrhage and colitic symptoms may be caused by necrosis of the intestinal mucous membrane secondary to involvement of the mesenteric arteries supplying the intestine; peripheral vascular manifestations including peripheral gangrene result from the involvement of peripheral arteries; signs of peripheral nerve disease are evidence of the disease having affected the arteries supplying the nerves involved; hemiplegic symptoms may be consequent to the rupture of an aneurysm of a cerebral artery.

P. S. Meyer originally described a triad of symptoms characteristic of periarteritis nodosa: (1) chlorotic marasmus (of Kussmaul and Maier); (2) polymyositis and polyneuritis, and (3) gastro-intestinal

symptoms (cramps, colic, sensitivity to palpation of the abdomen, signs of peritoneal irritation, loss of appetite, vomiting, diarrhea or constipation and bleeding from the gastro-intestinal tract). Subsequent observers (Brinkmann and Christeller) emphasized a fourth cardinal symptom, that of nephritis which may be evidenced by urinary findings (albuminuria and hematuria), edema, nitrogen retention in the blood and an elevated blood pressure.

The skin and subcutaneous tissues have been mainly affected in three ways in the various cases reported. Rashes, edema or subcutaneous nodules may be present. In some cases, the rashes have been hemorrhagic; in others, erythematous. Petechiae have been observed, and occasionally the hemorrhagic manifestations have gone on to necrotic ulcerations. These rashes have been regarded as of toxic origin. Edema has been observed in the majority of the cases reported, at times limited to the face and eyelids or to the hands and feet; often it has been generalized over the entire body. The edema is considered to be of nephritic origin, particularly in view of the high incidence of renal involvement by the periarteritic process. Subcutaneous nodules represent either thickenings in the wall of the blood vessels or actual sacculated aneurysms in the coats of the arteries. They are small firm pea-sized masses, feeling shotlike on palpation as they lie along the course of the artery, often quite superficial and usually painless. Occasionally they may be reddened and tender. Suppurative degeneration is unusual, although it does occur rarely, as in Klotz's second case in which examination of a nodule removed for diagnosis was of no help in establishing the diagnosis because of hemorrhage and extensive degeneration in the excised tissue, although on necropsy periarteritis nodosa was found. Pulsation has seldom been observed in these nodules (sacculated aneurysms), for thrombosis takes place early. Herlitz (1930) estimated their frequency of occurrence to be 12.5 per cent (in one eighth of the cases), whereas Manges and Baehr (1921) placed the figure at 25 per cent and Singer (1927) at 20 per cent. The apparent discrepancy may be explained by the increasingly larger number of cases reported in later years, especially those with only microscopic evidence of the disease, so that the actual number of cases in which subcutaneous nodules have been observed bears a smaller percentage relationship to the total number of cases reported.

Pain in the voluntary muscles and along the peripheral nerves is of frequent occurrence. It may be so pronounced a symptom as to cause one to suspect the possibility of polymyositis or trichinosis. Indeed, this occurred in our first case, and a biopsy of a piece of muscle tissue was resorted to. However, histologic examination revealed changes suggestive of periarteritis nodosa. Likewise, in the classic case which

gave the disease its name, Kussmaul at first thought that he was dealing with an unusual type of trichinosis until the development of atrophies and other symptoms convinced him of his error.

Pains in the joints may be present which, if sufficiently acute, may simulate an acute rheumatic fever, especially if several joints are involved. Lamb noted joint pains in 39 per cent of his series. Attacks of tonsillitis, sore throat or grip have been reported in many cases. Patients often refer the onset of their illness to an attack of sore throat. This has been well demonstrated in the cases of Manges and Baehr, Lamb and Klotz.

Harbitz classified periarteritis nodosa into six general clinical types: (1) gastro-intestinal; (2) renal; (3) neuromuscular; (4) cardiac; (5) cerebral, and (6) a form with pronounced changes in the skin. A "nervous" form has been added to the already numerous clinical types by Marinesco and Draganesco (who collected a number of cases from the literature and added another). It is obvious that any one case may be a combination of several of the types mentioned, for the apparently different types are in reality the result of the same disease process involving the arteries supplying the nerves, muscles or organs affected. The clinical symptom complex will, therefore, vary in accordance with the site affected.

Medically, cases of periarteritis nodosa have been diagnosed variously. The kidneys are so often involved (74 per cent incidence according to Gruber's figures) that hemorrhagic nephritis appears to be the most frequent diagnosis. To quote von Haun: "Cases have been regarded as trichinosis, as Werlhof's disease, typhoid fever, miliary tuberculosis, polymyositis, arteriosclerosis with sclerosis of the kidneys, neuritis multiplex, gastro-enteritis, pyemia, hemorrhagic nephritis, serositis tuberculosa, influenza with renal hemorrhage, purpura hemorrhagica." Bennett and Levine reported a case (their second) which simulated a chronic meningococcemia with clinical signs of meningitis. The spinal fluid was found to have a high leukocyte count, but repeated cultures of both spinal fluid and blood were sterile. Necropsy revealed typical lesions of periarteritis nodosa in the blood vessels of almost all of the organs.

The symptomatology may simulate an acute abdominal condition for which surgical intervention is deemed necessary—usually that of an acute appendicitis or an acute surgical condition of the kidney or of the gallbladder. In 2 of the 3 cases of periarteritis nodosa reported by Hauser, abdominal operations were done under mistaken diagnoses of acute surgical conditions of the kidney and in 1 nephrectomy was done on the left side. In the case of Manges and Baehr, laparotomy was performed for symptoms which were interpreted as those of

acute appendicitis. In Keegan's case, nephrectomy was done for pyonephrosis or pyelonephritis, but the operative specimen revealed the characteristic changes of periarteritis nodosa. In Gray's case the diagnosis was perinephric abscess, and decapsulation of the kidney was done. Five days later, death took place, and necropsy revealed periarteritis nodosa affecting the kidneys, heart, liver, spleen and mesentery. In Lamb's case, appendectomy was done, but the appendix was found to be normal. In some of the cases, shortly before death, a sudden collapse occurred; marked pallor and a thready pulse were observed, and signs of intra-abdominal hemorrhage became evident. In such instances necropsy revealed gross intraperitoneal hemorrhage secondary to a rupture of an aneurysm of the cystic artery, e. g., Gray's first case, or secondary to ruptured aneurysms of the liver, e. g., Klotz's two cases, Lemke's first case and Baló and Nächnebel's sixth case.

When the varied symptoms are numerous, the clinical picture may be so bizarre as to render a correct diagnosis during life extremely difficult. In fact, correct diagnosis in vivo is at best infrequent, the great majority of cases having been recognized only after necropsy. Should the case be one of the 12 per cent (Herlitz) in which local subcutaneous nodules are present, biopsy may be of value. However, at times, in cases later proved to be instances of periarteritis nodosa, histologic examination of a nodule has been unsatisfactory, e. g.: (1) Strong's case, in which the subcutaneous nodule removed at biopsy showed fibrosis and chronic inflammatory tissue around a moderately large artery, but the diagnosis of periarteritis nodosa could be made only after autopsy; (2) Klotz's second case, in which, after the excision of the subcutaneous nodule, a diagnosis of the arterial lesion could not be made owing to the extensive disintegration and hemorrhage in the excised tissue, although necropsy showed periarteritis nodosa. In 1922, Mertens reported that only 7 per cent of the cases have been recognized prior to death. (The total number of cases of periarteritis nodosa was stated as 70 by Ophüls one year later; consequently, the 7 per cent would represent 5 cases.) A positive intra vitam diagnosis has been made by excision and histologic examination of nodules in the skin or subcutaneous tissue to date in 12 cases—Kussmaul and Maier (second case), Benedict, Schmorl, von Haun, Carling and Braxton-Hicks, Kopp (pathologic report made by Lemke), Morawitz, Weigeldt, Macaigne and Nicaud, van Paassen, Goldstein (second case) and Lindberg. In the first of our 2 cases, excision of a piece of muscle tissue was done to rule out trichiniasis, and when histologic examination revealed periarteritic changes we were able to make a tentative diagnosis of periarteritis nodosa in vivo. In Manges and Baehr's case, a diagnosis in vivo was based on histologic examination of a mesenteric nodule

removed at laparotomy two months prior to death. In Gruber's case, cholecystectomy had been done four months prior to death for pain in the region of the gallbladder, high fever and chills, and histologic examination of the operative specimen of gallbladder and cystic artery revealed periarteritis nodosa of the cystic artery. In Goldstein's first case, gangrene of the left lower extremity necessitated amputation, and pathologic examination of the operative specimen confirmed the diagnosis of periarteritis nodosa in vivo. In Keegan's case, nephrectomy was done two months prior to death for a suspected surgical condition of the kidney, and histologic examination revealed periarteritis nodosa. Thus, in all, there have been 17 cases in which the diagnosis has been made in vivo based on definite histologic examination—or 8.7 per cent (in a total of 195 cases).

In 7 other cases in which there were no nodules, a tentative clinical diagnosis of periarteritis nodosa was made during life based on clinical symptomatology alone and was subsequently confirmed on necropsy—Sacki, von Spindler, Stepp (1 case), Reilly (in the case reported by Hutinel and co-workers), Silbermann (1 case), Bansi (the second case in his report) and Gohrbrandt (fourth case). In the latter group of cases the diagnosis must necessarily be considered only tentative or "possible" clinically, for had they not been confirmed by necropsy, such cases would be unproved. There have been several reports of cases deemed clinically to be instances of periarteritis nodosa, but without subsequent confirmation by necropsy or biopsy, and such cases we have not included because of lack of proved evidence of the actual presence of the disease (e. g., Ledoux, Cathala and Bœgner).

It is not within the scope of this paper to enter into a detailed pathologic discussion of periarteritis nodosa, for the subject has been adequately described in reports by various pathologists. We will merely concern ourselves with a brief description of the underlying vascular process sufficient to explain the resultant clinical effects. Periarteritis nodosa is characterized by necrosis of the media with fibrinous exudation. Associated with this are marked cellular infiltration and granulation tissue formation in and about the arterial wall together with varying degrees of proliferation of the intima. The inflammatory reaction in the intima results in endothelial desquamation and in a proliferative process obstructing the lumen. In some cases, obliteration of the lumen with subsequent canalization results; in others, aneurysmal dilatation of the vessel wall occurs. In either event, important disturbances in circulation result. Infarctions and localized hemorrhages due to aneurysmal rupture are frequently observed.

Death may be due to hemorrhage from the rupture of an aneurysm in a vital area, from necrosis or from an insufficiency of vital organs

resulting from the occlusion of the lumen of their arteries by thrombosis or the intimal proliferation. The extent of the obliteration present will determine the degree of the patency of the lumen of the vessels and therefore will regulate the volume of blood supplied to the organs involved. On the latter depends the degree of resultant atrophy and fibrosis of the tissue of that organ. If there is too marked a diminution in the blood supply of a vital organ, the resultant atrophy and fibrosis will be so extensive that the functional insufficiency of the organ will result in death as in cases of renal insufficiency reported by Veszprémi (second case), Lemke (third case), Wordley and Damblé. In our second case and that of Pickert-Menke, death was due to cardiac insufficiency. Cases of death from profuse hemorrhage secondary to the rupture of arterial aneurysms in various vital areas have been

TABLE 2.—*Localization of Pathologic Changes in Periarteritis Nodosa* *

	Times	Per Cent		Times	Per Cent
Kidneys	80	74	Skin and subcutaneous tissue	14	13
Heart	71	66	Bronchi	9	8
Liver	66	61	Brain	9	8
Stomach and intestines	50	46	Lungs	4	3.7
Mesentery and peritoneum	41	38	Lymph nodes	3	2.7
Musculature	32	30	Bladder and ureters	3	2.7
Pancreas	36	33	Spinal cord	2	1.8
Genitalia	21	19	Thyroid gland	2	1.8
Peripheral nerves	20	18.5	Pleura	2	1.8
Spleen	15	14	Mediastinum	2	1.8
Suprarenals	15	14	Sympathetic nervous system	1	0.9
Gallbladder	13	12	Synovial membrane of joints	1	0.9
Total cases				108	

* Tabulation of figures from Gruber's review of 108 cases (Zentralbl. f. Herz.-u. Gefässkr. **18**: 198, 1926).

described, as for example, in the brain (Dickson, Arkin, Kimmelstiel's second case, Veszprémi and Jancsó); in the lung (Sternberg); in the intestine (Lowenberg); in the abdomen from a ruptured aneurysm of the liver (Klotz's 2 cases, Lemke's first case, Baló and Nächtnebel's sixth case) and from a ruptured aneurysm of the cystic artery (Gray's first case); in the kidney (Schmidt, Harris and Friedrichs, Mertens, Walter and Fishberg), and in the pericardium (Vance and Graham).

The disease may involve any of the organs, and cases have been reported in which the process was found to be local and not general. In Hauser's first case, only one kidney was involved, whereas all of the other organs were microscopically free. In Brasser's case, the only organs involved were both kidneys. In the cases reported by Gruber, 108 were referred to in which mention had been made of the localization of the pathologic processes. Table 2 shows the incidence of involvement of the various organs.

The etiology of periarteritis nodosa is still unknown. Various theories have been advanced, but none has been universally accepted.

The disease originally was thought to be on a syphilitic basis (Kussmaul and Maier, Chvostek and Weichselbaum, Schmorl, Versé and others), but this view is no longer held tenable. Histologic studies have failed to show specific syphilitic lesions, and spirochetes have never been demonstrated in any of the tissue examinations. Gruber stated that in a series of 40 cases in which Wassermann tests had been made, 33 were negative, 4 were positive and the remaining 3 questionable. The much quoted case of Schmorl of a 53 year old patient with periarteritis nodosa in whom great improvement was noted after energetic antisyphilitic treatment loses its significance in view of the definite proof of arterial healing noted in such cases as those of Manges and Baehr and Arkin (fifth case) in which antisyphilitic treatment had never been given and yet in which arterial healing had been progressive.

Some authors have assumed a morphologic, constitutional defect or weakness which would supposedly lessen the resistance to the noxa producing periarteritis nodosa. Eppinger was of the opinion that a congenital weakness of the media, and especially of the elastica interna, was present. Pertik and Benda favored the theory of a primary mechanical damage. Among the cases of periarteritis nodosa reported in the literature up to 1920, Kroetz found an aorta angusta 6 times, a patent foramen ovale once and fatty degeneration of the elastica interna in one quarter of the patients under 30 years of age.

Most modern authors believe periarteritis nodosa to be a sepsis, but a great deal of controversy exists as to whether or not a specific causative organism is concerned. The proponents of the specificity of the causative organism in turn differ as to whether a filtrable virus or a nonfiltrable micro-organism is at fault. In addition, the very pathogenesis of periarteritis nodosa has been interpreted as extremely suggestive of an infectious origin, for the early cases show acute inflammatory changes, which, if time permits, develop fibrosis and sclerosis as an attempt toward healing (e. g., Manges and Baehr's case; Arkin's fifth case). However, in all of the cases reported, repeated blood cultures and all other cultures and bacteriologic investigations on material taken from subcutaneous nodules or from various organs at necropsy have failed to show any specific causative agent. In the case of Bennett and Levine which simulated a chronic meningococcemia with meningitis repeated cultures of both blood and spinal fluid were sterile.

Transmission to animals has been attempted repeatedly. Von Haun claimed to have reproduced lesions similar to those occurring in human cases by injecting the patient's blood into guinea-pigs and carrying on from the original series into a second series of guinea-pigs. Harris and Friedrichs reported typical changes of periarteritis nodosa in a rabbit following an intravenous injection of a filtrate prepared from the

organs of another rabbit that had been killed ten weeks after having been inoculated with a suspension made from the nodules of a human case. In their opinion, the disease is due to a specific filtrable agent. However, Sadao Otani could not repeat these experiments, and Franz failed to reproduce the disease in guinea-pigs. Studies of lesions similar to those of periarteritis nodosa in man occurring in the deer, calf, pig and dog have not cleared the situation.

Gruber, on the other hand, expressed the belief that periarteritis nodosa is not a disease sui generis, but that patients with this condition have had an increased sensitivity of their arteries from a previous infection and that the arterial lesions are the result of a hyperergic (allergic) reaction to various infectious or damaging agents (Erfölgsreizung).

Spiro maintained that the lesions found in periarteritis nodosa differ only quantitatively from those encountered in many infectious diseases—like measles, scarlatina and diphtheria. Both Gruber and Spiro expressed the opinion that the diseases thus far designated as periarteritis nodosa actually belong in a group of processes of "mesarteritis." It may be of interest to note in passing that the presence of eosinophils in various sites in striking numbers in some cases (e. g., in those of Gray, Lewis, Lamb) suggests a point in favor of the allergic theory of a variety of causative agents. At least, the striking eosinophilia in the cases mentioned taken with the complete absence of eosinophils in so many other cases casts doubt on the complete uniformity of type of lesion which is one of the features emphasized by those who believe a specific ultravirus to be the causative factor (Baló; Marinesco and Draganesco).

It has been thought by some investigators that rheumatic infection might play an etiologic rôle because of the frequent association of periarteritis nodosa with sore throat, arthritis, muscle pains, certain of the cutaneous rashes and leukocytosis—all of which would suggest an infection—possibly of the rheumatic type (Klotz and Ophüls). In view of the suggestion of Swift and his co-workers that rheumatic fever itself may possibly be a hyperergic reaction to a nonhemolytic streptococcus, and in view of Gruber's theory of the allergic etiology of periarteritis nodosa, the possible connection between periarteritis nodosa and rheumatic fever is of great interest. In our second case, both conditions were found to be coexistent at necropsy—on both gross and microscopic examination. However, just what relationship, if any, the two conditions bear to each other is a matter of conjecture at present. In view of the frequency of rheumatic infection in New York, the presence of the two diseases in the same person may be merely coincidental.

In our opinion, the name periarteritis nodosa is a misnomer, for it would lead one not cognizant with the manifestations of the disease

to expect to find nodules either subcutaneously or macroscopically along the course of the arteries at necropsy. Herlitz found subcutaneous nodules present in only one eighth of the cases in the literature, and a number of cases are now on record in which not only were there no subcutaneous nodules but there was no gross evidence of the presence of the disease at necropsy. In fact, only a careful microscopic examination revealed changes of periarteritis nodosa (Meyer, Veszprémi, Wohlwill, Gray, Bansi, Silbermann, 3 of the 4 cases reported by Kimmelstiel, Lemke [third case], Gruber [14 year old child], Frommel, Holterman, Marinesco and Draganesco and Hinrichs). Thus, if one bases the diagnosis only on the presence of the characteristic nodules subcutaneously or on the presence of gross periarterial nodules or thickenings of the vessel walls on sectioning the organs at necropsy, it is obvious that a number of cases will be completely missed or not classified within this disease group. Certainly a careful and extensive microscopic examination of all of the organs is vitally necessary before the pathologist can declare the disease absent. Consequently, it would seem wiser not to confuse the picture of the disease by labeling it with a name which does not apply to the entire group. Possibly "periarteritis," which can be in turn divided into acute, subacute or chronic stages, would be a more fitting term until the etiologic factors are discovered. At present, it is our view that the diseases which have been previously termed periarteritis nodosa are really similar syndromes or symptom complexes, possibly caused by allergic reactions to several different factors or infectious agents.

REPORT OF CASES

CASE 1.—*History.*—S. M., a 10 year old boy, previously healthy, was admitted to the pediatric service of Mount Sinai Hospital on Oct. 2, 1923, with a history of having had pain in both upper and lower extremities for the previous ten weeks. During the four weeks prior to admission, he had been confined to bed because of increasing pain and fever. Physical examination on admission revealed a poorly developed boy complaining of pain in all four extremities. The skin showed no eruption. The pharyngeal mucosa was injected, and the tonsils were hypertrophied. Examination of the lungs and heart gave completely negative results. The pulse rate was 124; the temperature, 101.4 F., and respirations, 28. There was no spasm, tenderness, rigidity or palpable masses on abdominal examination. The spleen was just palpable, and the liver was not enlarged. The kidneys were not felt. Any attempt of motion of both upper and lower extremities was painful, but there was no evidence of actual involvement of the joints. Neurologic findings were entirely normal. Urinalysis gave negative results, no albumin, casts or cells being present. Leukocytosis, with 11,000 leukocytes and 80 per cent polymorphonuclears, was present.

During the patient's first four months in the hospital, the most prominent symptoms were pain in the muscle of the upper and the lower extremities, leading to muscular atrophy with resultant contractures. The joints were not involved.

Clinically, polymyositis and trichinosis were considered. Finally, a small piece of muscle from the right arm was excised for biopsy, and histologic examination revealed dilatation of vessels with perivascular infiltration of polymorphonuclear cells; the muscle fibers were normal (fig. 1).

The course remained persistently febrile, the temperature becoming elevated to 103.2 F., with an accelerated pulse rate. There was some leukocytosis with occasional polynucleosis. The urine was generally normal, and on only a few occasions showed traces of albumin and occasional white blood cells. Chemical examination of the blood showed normal figures. The blood cultures were sterile. The Wassermann tests of the blood and cerebrospinal fluid were negative. The blood pressure was elevated during the last two months of the illness, the systolic pressure varying between 145 and 170 with the diastolic between 112 and 135. Roentgen

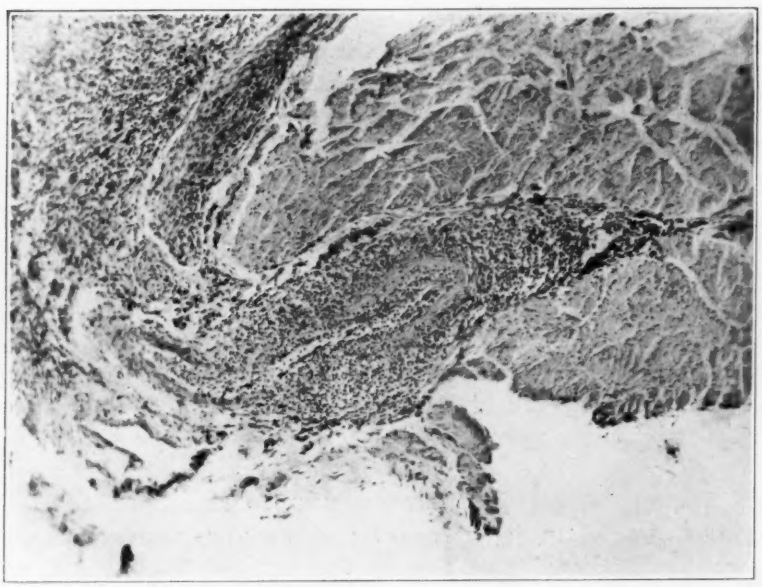

Fig. 1 (case 1).—Photomicrograph of an artery in a section of muscle tissue taken for biopsy. The left side is normal; the right side shows proliferation and infiltration of the intima, a hyaline fibrinoid ring of media and adventitial infiltration. Reduced from a magnification of × 100.

examination of the thorax, pelvis and both upper and lower extremities did not show any evidence of abnormality.

During the patient's fifth month in the hospital, he was presented at a clinical conference at the Mount Sinai Hospital (February, 1924), the presentation being made under the caption of "A Case for Diagnosis; Tentative Diagnosis of Periarteritis Nodosa." The tentative diagnosis was based on the bizarre clinical picture and the strongly suggestive evidence obtained by histologic examination of the piece of muscle tissue removed for biopsy.

Beginning in the fifth month after admission, the patient was seized with repeated severe attacks of generalized convulsions with loss of consciousness and incontinence of feces and urine. Lumbar puncture made repeatedly elicited clear

fluid under normal pressure; the cell count was not increased. He gradually recovered from these seizures with vastly deteriorated sensorium and loss of memory. Six weeks before death, left-sided orchitis developed, with swelling of the testicle and marked sensitiveness on palpation. Death occurred on March 27, 1924, after a total illness of eight months' duration.

Necropsy.—Macroscopic Examination: The pleural cavities were normal. The lungs weighed 576 Gm. They were uniformly pinkish red and on section showed brownish induration. The heart weighed 250 Gm. and was slightly larger than normal. The cavities, valves and amount of fluid in the pericardium were all normal. The appearance of the heart was striking and unusual. Along both coronary vessels, especially the descending rami on both anterior and posterior aspects of the heart, were numerous protuberances beneath the visceral pericar-

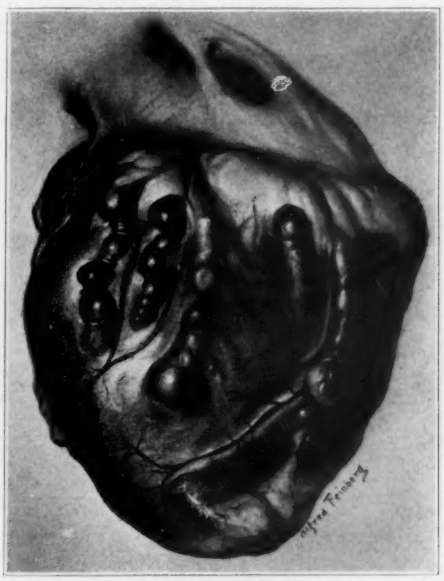

Fig. 2 (case 1).—Photograph of the heart (posterior surface) showing nodules on the branches of the coronary artery.

dium varying in size from that of the head of a pin to that of a pea, the largest being the size of small grapes. These nodules, apparently sacculated aneurysms, were bluish red and were arranged in almost a continuous row along the branches of the coronary arteries as though they were strings of irregularly sized beads (fig. 2). The veins seemed uninvolved.

The liver weighed 900 Gm., was larger than normal in size and appeared to be irregularly mottled, with vaguely outlined yellowish patches on a granular, reddish background. On cross section, the nutmeg appearance of passive congestion was seen. In several places, small branches of the hepatic artery lining Glisson's capsule appeared to be irregularly thickened. Nodules of thickening were seen along some of the main branches of the hepatic artery and seemed especially conspicuous along the cystic artery.

The kidneys together weighed 180 Gm. and seemed normal in size. Their capsules stripped easily, revealing a surface of unusual appearance. The pinkish sur-

faces were irregularly mottled with yellowish streaks and brownish-yellow, slightly depressed, areas of fairly sharp outline. On section, they appeared to extend more or less deeply into the renal cortex. Deeper in the cortex were some very fine yellowish streaks and patches. These areas appeared to be those of necrosis. The only renal vessels showing evidence of the disease were the interlobular branches which were irregularly thickened in several places.

The suprarenals revealed no gross evidence of the disease except for a minute, barely macroscopic nodule on one small branch of the artery to the right suprarenal. The spleen weighed 120 Gm. and seemed slightly larger than normal. On

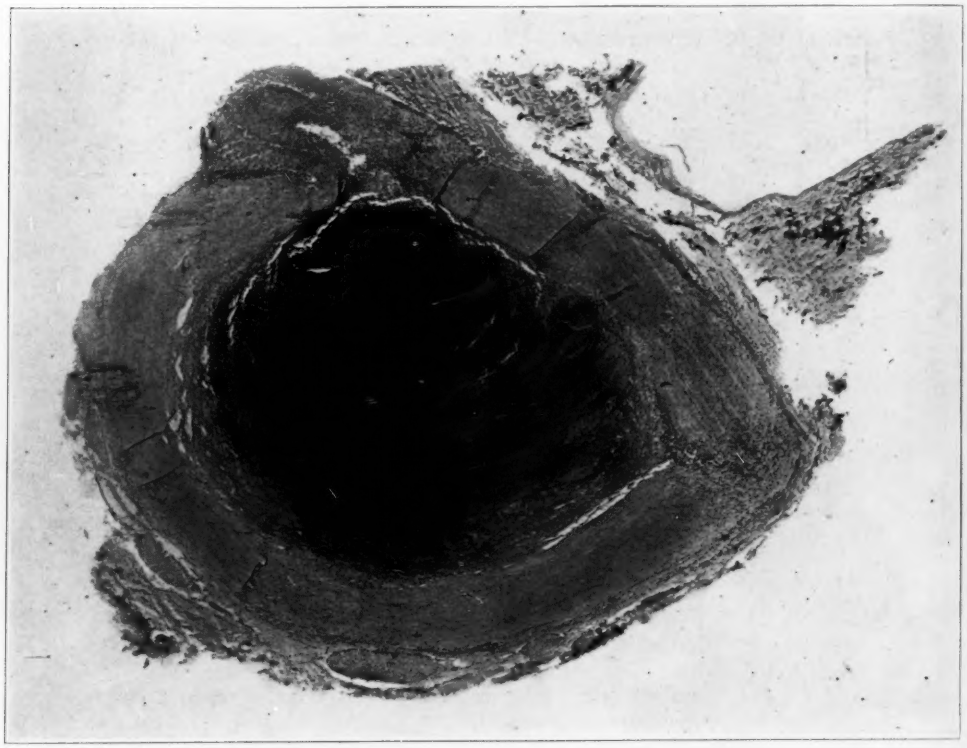

Fig. 3 (case 1).—Photomicrograph of the intrahepatic artery (a section of the whole artery) showing an aneurysm in one area with a red thrombus in the lumen; × 20.

cross-section, it presented a homogeneous fleshy appearance, no malpighian bodies being visible. The splenic vessels seemed normal. The pancreas appeared normal save for occasional small areas of necrosis.

The stomach appeared uninvolved save for a bluish, pea-sized nodule lying beneath the submucosa in the center of the posterior wall about 1 inch from the lesser curvature. The nodule was best seen from the mucosal surface on which it produced a distinct projection. It was removed for microscopic section. The mesentery of the small intestines was filled with irregularly enlarged lymph nodes, pea-sized, pinkish and moist on section. The mesenteric arteries appeared to be grossly free of the disease until one reached the minute, barely visible branches

which entered the serosa of the small intestine near the mesenteric attachment. At this point, on ten or twelve of such branches, minute aneurysms were seen, some being barely visible and others being as large as a grain of barley. A few were dense and yellowish white as though organized. The large intestine showed no gross evidence of disease.

The left testicle appeared somewhat smaller than the right but was grossly normal. It was removed for microscopic section.

Microscopic Examination: There were areas of degeneration of muscle fibers; the arteries showed changes of periarteritis nodosa.

Fig. 4 (case 1).—Photomicrograph of a medium-sized artery of the pancreas. The lamina elastica interna is torn with the ends rolled outward; the media is destroyed to the greater part and replaced by fibrous tissue; there is very marked intimal proliferation with nearly complete obstruction of the lumen. Elastica-carmine; reduced from a magnification of × 60.

There was marked round cell infiltration in the periportal spaces of the liver, the parenchyma being fairly well preserved.

The hepatic artery showed periarteritis nodosa.

There was complete occlusion of the intrahepatic artery due to thrombosis resulting from periarteritis nodosa (fig. 3).

No evidence of the disease process was seen in the cystic artery (although grossly the vessel walls had seemed somewhat thickened).

A large periarteritic nodule involved all of the coats of the wall of the stomach.

In the mesenteric artery was a miliary aneurysm formation as a result of the periarteritic process.

Numerous very small malpighian follicles were seen in the spleen; there was marked hyperplasia of the reticulum.

The pancreas showed marked increase in the interacinar connective tissue; one blood vessel showed evidence of healed periarteritis nodosa with marked narrowing of the lumen (fig. 4); some of the smaller vessels revealed miliary aneurysm formation.

Large areas of focal degeneration were seen in the parenchyma of the kidneys with calcium deposits in the tubules; there was marked involvement of the larger branches of the renal artery by periarteritis nodosa.

The testicle showed fibrosis and atrophy of the tubules.

Small vessels around the suprarenal revealed evidence of periarterial inflammatory changes.

Comment.—From the symptoms presented, this case belongs to the neuromuscular type of periarteritis nodosa. Besides the long duration of the fever and the accelerated pulse rate, a point of interest lies in the paucity of cardiac and renal symptoms when compared with the extensive lesions in these organs after death. Also noteworthy is the orchitis which has been observed in only a few cases.

This case was the first instance in a child of the recognition of the disease in vivo at the time when the patient was presented at the monthly clinical conference of the Mount Sinai Hospital in February, 1924, one month prior to death. Since no subcutaneous nodules had been observed in this child, although histologic examination of the piece of muscle removed at biopsy showed changes strongly suggestive of periarteritis nodosa, it was felt that a clinical diagnosis in vivo must necessarily remain only tentative or presumptive unless histologic examination of a subcutaneous nodule, of a mesenteric nodule (as in Manges and Baehr's case) or of a piece of artery were to confirm the diagnosis and render it positive. This tentative clinical diagnosis in vivo was later confirmed at necropsy. A brief report of this case was made four years later by Dr. Welt at the meeting of the New York Pathological Society on April 12, 1928.

CASE 2.—*History.*—R. S., a 7 year old schoolboy, was admitted to the Mount Sinai Hospital on March 20, 1931. His previous history was completely without significance save for pertussis at 2 years of age, measles, chickenpox and mumps at 3 years of age; except for infrequent colds, the child had been otherwise well until the present illness. He had never experienced any joint pains, chorea or severe sore throat and had never had any cardiac symptoms.

Eight weeks prior to admission, the child had a mild attack of scarlet fever with desquamation taking place during the second week of illness. At the beginning of the third week the child became febrile, and a cervical adenitis was found. Three days later, the temperature rose to 103 F., and he experienced attacks of severe cramplike pain in the epigastrium which lasted for from ten to fifteen minutes at a time and came on every half-hour. The fever, abdominal pain and cervical adenopathy lasted for from four to five days, and by the end of the third week of illness had disappeared. The child then began to complain of pain in the ball of the right foot and in the right thumb, and finally in the groin. The pain

was transient, migratory and aching and lasted throughout the fourth week, but was not accompanied by redness or swelling. A slight limitation of motion seemed due to pain. The cardiovascular system had been normal up to this time. Subsequently, he began to complain of pain in the scrotal region which did not seem associated with any urinary symptoms. About this time (two or three weeks prior to admission), dyspnea, weakness, pallor and slight cough became evident and gradually increased. A diagnosis of "rheumatic heart disease" was made, and the child was hospitalized. There had been no edema of the extremities, abdomen or scrotum.

Physical examination on admission revealed a moderate dyspnea, pallor and slight cyanosis. The temperature was 106 F.; the pulse rate, 124, and respirations, 68. The heart was enlarged to the left, and there were evidences of a mitral lesion. The liver was slightly enlarged, but the spleen was not palpable. Examination of the chest revealed dulness with râles at both bases. A diagnosis of rheumatic cardiovalvular disease and rheumatic endocarditis was made.

The blood count revealed a hemoglobin of 70 per cent, with 5,000,000 red blood cells and 16,000 white blood cells, with a differential count of 81 per cent polymorphonuclears, 17 per cent lymphocytes and 2 per cent mononuclears.

A roentgenogram of the chest showed marked enlargement of the left ventricle and a diffuse mottling of both lungs, most marked at the base, which was interpreted by the roentgenologist as a marked congestion secondary to mitral disease. The child was digitalized, and salicylate medication was given. The temperature ranged up and down between 100 and 103 F., although at times rising as high as 105 F. The pulse ranged between 116 and 156, with respirations varying between 24 and 40. The general condition did not improve. The pulse remained regular but was poorly sustained. Examination of the chest from day to day revealed râles at the base of both lungs. The child's condition rapidly grew worse. The liver became enlarged until the lower edge was palpable 6 cm. below the costal margin. The cyanosis increased, and the dyspnea became extremely severe. The pulse grew feeble and finally thready and irregular prior to death. Repeated blood cultures gave negative results. The urine remained completely normal throughout the course of the disease. Two days prior to death the hemoglobin had dropped to 38 per cent with 2,500,000 red blood cells. Slight edema developed. It was felt that the heart had rapidly become decompensated secondary to the cardiovalvular disease. Death finally took place three weeks following admission, after a total duration of illness of approximately nine weeks.

Necropsy.—Macroscopic Examination: The right pleural cavity was found to contain about 500 cc. of a thin, straw-colored fluid without fibrin. Cut section of the lungs showed numerous streaks about the diameter of a cotton thread spreading out from the hilus of the lung which, when cut across, revealed thickening of the walls of branches of the pulmonary arteries. A fine lacework of whitish streaks with a miliary nodular appearance was observed throughout the parenchyma of all of the lobes of the lung.

The heart weighed 550 Gm. (including the pericardium and about 50 cc. of pale, yellowish fluid). The pericardium seemed roughened and granular in the region of the pulmonic artery but was smooth and glistening elsewhere. The left and right ventricles were slightly enlarged. The myocardium was soft and flabby but not hypertrophied, and there was moderate tigerization of the endocardium. The tricuspid and pulmonic valves were normal. Examination of the mitral valve revealed an uneven shelflike formation extending almost the entire length of the closure line and measuring about from 2 to 3 mm. in height. On the posterior flap in this closure line were numerous, tiny, grayish-white verrucae. A few of

these verrucae were also present on the aortic flap. There were no verrucae or other vegetations either on the slightly thickened chordae tendinae or on the walls of the auricle or ventricle. Grossly, the appearance was that of a subacute-verrucous rheumatic endocarditis.

The branches of the right coronary artery, especially the right marginal, were distinctly thickened, and in one place nodular on palpation.

There were no nodules on the surfaces of the liver. Cut section revealed an indistinct lobular structure and a cloudy swelling. Several cross-sected blood vessels seemed thicker than normal. The gallbladder, suprarenals, spleen and pancreas were grossly normal.

The kidneys were normal in size with the capsules stripping easily from a smooth surface. There were numerous reddish areas of varying size and shape, which on cut section were seen to correspond with reddish streaks in the cortex. The medulla seemed normal. Branches of the renal artery were found to be distinctly thicker and more rigid than normal at their entrance to the medullary-pelvic junction. The kidney pelvis, bladder and ureters were normal.

The gastro-intestinal tract was normal save for the prominence of the lymphoid follicles in the terminal ileum and part of the ascending colon. The lymph nodes of the mesentery of the small intestine were slightly enlarged. The peritoneal surfaces of the stomach and loops of intestine did not reveal any hemorrhage or nodules. The mesenteric vessels were grossly normal.

The aorta seemed slightly narrowed, but there were no other changes. A branch of the external iliac artery was found difficult to probe and was fixed in preparation for sectioning.

Microscopic Examination: The lungs showed a most extensive involvement of the arteries by a necrotizing process with recent and old lesions; the alveoli contained edema, large mononuclear cells and numerous foci with fibrin.

The heart showed many typical Aschoff bodies within the interstitial tissue stroma.

The branches of the coronary artery showed old periarteritic lesions.

There were old arterial lesions in the liver with canalized thrombi.

There was a conspicuous increase of the cytoplasmic reticulum in the spleen and only two sections showed arterial changes.

The pancreas was normal save for changes in several of the arteries.

The stomach showed typical arterial changes within the subserosa; two of the arterial branches revealed intimal proliferation, fibrinoid necrosis of the inner media and adventitial infiltration.

The intestine was normal.

The tubular epithelium of the kidney was swollen, but the glomeruli with few exceptions were intact; all of the sections showed severe acute and chronic arterial changes, the involved arteries being the interlobar and interlobular vessels—the inner layer of the media presented a fibrinoid appearance with a marked periarterial infiltration of lymphocytes, polyblasts and a few polymorphonuclear leukocytes; the subendothelial layer was thickened and consisted of fibrinoid, necrotic material which, being frequently organized, resulted in a considerable narrowing of the lumen; the internal and external layer and the muscularis were focally destroyed in many places and were replaced by granulation and scar tissue formation.

Several of the veins showed parietal thrombi, apparently by propagation, the wall of the vein having become inflamed.

The suprarenal showed many older arterial lesions in the capsule.

There were old arterial changes in the diaphragm; one vein was thrombosed. The branch of external iliac showed periarteritic involvement.

Thus necropsy revealed the presence of rheumatic cardiovalvular disease with verrucous vegetations on the mitral and, to a slight extent, on the aortic valves, and with Aschoff bodies in the myocardium on microscopic examination. Grossly, there were changes of periarteritis nodosa involving the lungs, branches of the right coronary and branches of the renal artery, while microscopically, changes of periarteritis nodosa were observed in the lungs, liver, stomach, diaphragm, coronary artery, renal arteries, arteries in the suprarenal capsule, the branch of the external iliac artery, the arteries of the pancreas and the spleen on several sections.

Comment.—From the symptoms presented, this case belonged to the cardiovascular type of periarteritis nodosa. It is particularly interesting and rare because of the coexistence of both periarteritis nodosa and rheumatic heart disease as proved on necropsy. Clinically, the case had seemed one of rheumatic cardiovalvular disease with rapid decompensation, death being due to cardiac failure.

As stated before, it is interesting to speculate as to the possible connection between the two diseases. Bearing in mind Swift's theory of the possible allergic basis of rheumatic fever (allergic to the streptococcus), and Gruber's theory of the sensibility of the blood vessels secondary to some infectious agent with the lesions of periarteritis nodosa resulting from the hyperergic reaction of the blood vessels, this case may represent a possible connecting link between the two diseases. The rheumatic fever, if really on an allergic basis, might sensitize the vessel walls to the streptococcus and the resulting hyperergic reaction give rise to the lesions of periarteritis nodosa. Such a statement can, of course, be only speculative, though interesting. It is rather surprising to note no abnormal urinary findings in this case, although on necropsy the vessels of the kidney were found severely involved. However, the glomeruli and tubules apparently were not markedly involved, perhaps because the renal arterial involvement had not been sufficiently extensive to interfere with the blood supply to the organ.

We have felt that it would be of interest to append to this paper abstracts of all the known, proved cases of periarteritis nodosa in children up to 15 years of age. In all, we have been able to gather 21 cases from the literature. We have arranged the cases in table form, adding the two herein reported, so that the points of main significance may be more easily observed (table 3).

ANALYSIS OF CASES

Of the 23 cases in infancy and childhood, 2 occurred during the first year of life, 4 between the third and seventh years and 17 between the tenth and fifteenth years. The sex is known in all but 2 of the cases, and our figures show a proportion of 13 males to 8 females (62 and 38 per cent, respectively), or a ratio of 1.6 males to 1 female, in contradistinction to the figures of 4 males to 1 female given for the disease

TABLE 3.—*Data on*

Author and Year	Age of Child, Sex	Duration of Illness	Pulse Rate	Temperature	Blood Pressure	Red Blood Cells	White Blood Cells	Urine
Kundrat, 1875; quoted by Eppinger, 1887	10 ♀	Clinical history unknown except for the occurrence of marasmus; heart				.....	.....	.....
Krzyszkowski, 1899; quoted by Ferrari, 1903	2½ mos.	11 days	..	40 C.	..	.....	.....	.....
Veszprémi and Jancsó, 1903	14 yrs. ♂	6 mos.	On admission: 96 For 30 days prior to death: 140-156	39.2 C. 38-40 C.	.. ..	.....	.....	Albumin, ++; W.B.C., +; casts, many
Dickson, 1908	14½ yrs. ♂	10 wks.	On admission: 98 Two days later: 140	101 F. 102.2 F.	.. ..	Anemia present (figures not given)	Normal	Albumin, trace
Veszprémi (second case), 1912,	10 yrs. ♂	3 wks.	..	....	..	.....	.....	.....
Lamb (second case), 1914	10 yrs. ♀	5-6 wks.	74 120	99 F. 103.2 F.	Between 104 and 60	.....	Admission: 33,100 with 93% polymorphonuclears On 10th day: 26,200 with 92% polymorphonuclears On 16th day: 66,000 with 95% polymorphonuclears On 27th day: 26,600 with 88% polymorphonuclears	Albumin, faint trace; casts, few; no R.B.C.
Pickert-Menke, 1920	13 yrs. ♂	9-10 wks.	110-130 At end 70	37 C. or less	..	Fourth week of illness: 2,240,000 with hemoglobin 64%	48,300; predominance of polymorphonuclears; few myelocytes; eosinophils present; many nucleated red cells (figures of differential not given)	Albumin, +
Lemke (first case), 1922	11 yrs. ♂	6 wks.	120	40 C.	..	.....	.....	.....
Lemke (third case), 1922	5 yrs. ♂	4 wks.	...	....	115	.....	.....	Albumin, ++; casts, few; R.B.C., few
Wordley, 1923	13 yrs. ♂	8 wks.	100	101 F. irregular	106	.....	16,200; polymorphonuclears, 82%; lymphocytes, 14%; monocytes, 2%; eosinophils, 2%	Albumin, +; R.B.C., few; W.B.C., few; casts, few
Gruber, 1923	14 yrs. ♂	7-8 wks.	100	38 C. irregular	150 to 165	At onset: hemoglobin, 35% Later: hemoglobin, 25%	Three weeks after onset: 22,000 At death: 19,000	Albumin, ++; casts, granular and hyaline; W.B.C., few; R.B.C., many

Abdominal Pain	Liver	Spleen	Skin Manifestations	Sore Throat	Arthritis	Addenda	Clinical Diagnosis vs. Necropsy
....	..	..	.....	....	....	.....	Clinical diagnosis: marasmus ? Necropsy specimen: Heart showing multiple aneurysms of the coronary arteries with thrombosis
had been preserved as a museum specimen; later examined by Eppinger							
....	..	..	+ Edema	....	....	Edema of eyelids and extremities	Clinical Diagnosis: scarlet fever or syphilis Necropsy: (1) bronchopneumonia; (2) periarteritis nodosa, small nodules on coronary arteries
....	..	..	+ Urticaria; petechial hemorrhages, subcutaneous	....	....	Edema of feet; convulsions with coma; spinal tap, bloody	Clinical diagnosis: meningitis ?; cerebral hemorrhage ? Necropsy: (1) periarteritis nodosa of heart, stomach, intestines; multiple miliary aneurysms with thrombosis on coronary artery; (2) large meningeal hemorrhage
+	0	0	.....	....	....	Sudden onset with abdominal pain; semicoma; convulsions; spinal tap negative except for increased pressure	Clinical diagnosis: tuberculous or pneumococcal meningitis Necropsy: periarteritis nodosa; nodules on small and medium-sized arteries of heart, liver, spleen, kidneys, mesentery, brain, spinal cord; hemorrhage of brain
....	..	..	Edema; skin rash on 11th day of illness	....	....	Sudden onset with headache and increasing edema of face and eyelids; persistent vomiting; lethargy; convulsions; death 3 weeks after onset	Clinical diagnosis: acute glomerulonephritis with terminal uremia Necropsy: periarteritis nodosa; nodules in ventricles of heart, stomach, intestine and bladder; kidneys revealed presence of a subacute glomerulonephritis
++	0 +	0	+ Mottled dusky erythema	+	++	Wassermann, +++; laparotomy for acute appendicitis, but both appendix and peritoneum normal; postoperatively, sore throat, joint pains and nephritis developed	Clinical diagnosis: (1) on admission, acute appendicitis (but on laparotomy, appendix normal) (2) postoperatively, acute tonsillitis with secondary nephritis and polyarthritis Necropsy: periarteritis nodosa of heart, kidneys, liver, spleen and pancreas
++	++	0	..... Edema, ++	..	+	Edema, ++; muscular atrophy, ++; convulsions with periods of loss of consciousness; gradual circulatory failure with death from cardiac insufficiency	Clinical diagnosis: (1) at first, pus in the left kidney (puncture done, unsuccessful); (2) later, muscular atrophy or neuritis (during fourth week of illness) Necropsy: periarteritis nodosa; macroscopic nodules on the coronary arteries of the heart; microscopic, periarteritis nodosa of kidneys, heart, liver, lungs, spleen, intestines, pancreas
++	..	..	.....	"Grip"	..	Vomiting with abdominal pain; laparotomy done, but no pathologic process found, only clear fluid; sudden collapse 4 weeks postoperatively with death	Clinical diagnosis: "acute abdomen" (simulated an acute surgical abdominal condition with tenderness in lower part of abdomen; distention; no passage of gas) Necropsy: periarteritis nodosa; multiple aneurysms of arteries of the epicardium, myocardium, liver, right suprarenal capsule and both kidneys; 1,800 cc. bloody fluid in abdomen from walnut-sized aneurysm perforated through under surface of liver
Indefinite pains	..	..	..... Edema, ++	+++	..	Generalized edema; anuria; restlessness; finally convulsions with coma	Clinical diagnosis: acute nephritis with uremia Necropsy (permission limited to the removal of the right kidney only): (1) subacute glomerulonephritis; (2) periarteritis nodosa of the right kidney (on microscopic examination only)
++	..	..	0	0	0	No edema; eye-grounds normal; blood urea, 22 mg. per 100 cc.; repeated convulsions	Clinical diagnosis: (1) at first, renal calculus; (2) later, kidney neoplasm Necropsy: (1) periarteritis nodosa of heart and kidney; (2) cortical necrosis of kidney
....	+	+	0 Edema, +	++	....	Edema, +; pain in back; bilateral tonsillar abscesses incised and drained; culture of pus, streptococcus	Clinical diagnosis: (1) acute nephritis secondary to sore throat; (2) tonsillar abscesses with secondary sepsis Necropsy: periarteritis nodosa found only on microscopic examination of gallbladder and liver (other organs had not been examined microscopically)

TABLE 3.—*Data on Cases*

Author and Year	Age of Child, Sex	Duration of Illness	Pulse Rate	Temperature	Blood Pressure	Red Blood Cells	White Blood Cells	Urine
Thinnes, 1924	9 mos. ..	4 hrs.	...	.....	..	.....	.....	.....
Gray, 1926	12 yrs. ♂	9 wks.	136	102 F.	..	.....	.....	.....
Kimmelstiel (second case), 1927	10 yrs. ♀	3½ mos.	...	a.m. 37.5 C.; p.m. 38.5 C.	..	.....	10,000 with normal differential (figures not given)	.....
Basch, 1927	13 yrs. ♀	4 mos.	...	39.5 C. intermittent	.. 15th wk.: 165	4,280,000 with hemoglobin, 68%	10,800, with polymorphonuclears, 66%; lymphocytes, 24%; monocytes, 7%; basophils, 1%; eosinophils, 2%	Fifth week: Albumin, +; casts, rare; W.B.C., few 15th week: Albumin, +++; casts, numerous; R.B.C.
Baló and Nächtnebel (fourth case), 1928	14 yrs. ♂	5 wks.	...	No fever	..	.....	.....	.....
Debré and co-workers, 1928	3 yrs. ♂	2 wks.	100	38.4 C. to 39 C.; later 37 C. 36.2 C.	..	.....	.....	Albumin, ++; W.B.C., many; R.B.C., many

Abdominal Pain	Liver	Spleen	Skin Manifestations	Sore Throat	Arthritis	Addenda	Clinical Diagnosis vs. Necropsy
+	..	..	.....	+	....	Sudden onset 4 hrs. prior to death with apparent abdominal pain; physical examination merely revealed a reddened throat	Clinical diagnosis: acute pharyngitis Necropsy: periarteritis nodosa; macroscopic, dilated heart swellings or nodules and multiple kidney infarcts; microscopic, periarteritis nodosa involving the heart and kidneys
....	..	..	.....	..	++	Onset with infection of left thigh following injury; for 1 mo. thereafter, pain, tenderness, redness and swelling of thigh and inguinal region, lymphadenitis; blood cultures, sterile; involvement of other joints, painful; sudden collapse with death	Clinical diagnosis: posttraumatic cellulitis of left thigh with inguinal lymphadenitis Necropsy: periarteritis nodosa; aneurysmal dilatations and arterial changes in intrahepatic branches of hepatic arteries, smaller branches of renal and coronary arteries; death due to rupture of an aneurysm of cystic artery with peritoneal hemorrhage
++	..	..	.....	..	....	Onset with abdominal pain for 14 days associated with vomiting during last 2-day period; appendicectomy done but appendix normal; 3 mos. later, sudden convulsions with tonic twitches on left side; death on same day	Clinical diagnosis: (1) acute appendicitis (but on laparotomy, appendix found normal); (2) 3 months postoperatively, ? cerebral hemorrhage Necropsy: periarteritis nodosa involving myocardium, kidneys, gallbladder, pancreas, spleen, stomach, intestines, uterus, ovaries, vessels in peripheral nerves, bladder; death due to cerebral hemorrhage from rupture of an undiscovered cerebral aneurysm
+ ++	..	At first + Later: ++	During 4th wk.: macular rash sparsely distributed over the trunk and extremities; transient; slightly livid in color	"Grip" at onset	During 4th wk. + Later: ++; polyarthritis	Onset with "grip"; during 4th wk., onset of abdominal pain, joint pain, fever and vomiting; blood culture, sterile; pain along spine and sacrum as well as polyarthritis; in 15th wk., uremia of eclamptic type; urine markedly involved; blood pressure high, eyegrounds normal; death in middle of 17th wk. with signs of kidney insufficiency and terminal pneumonia; Pirquet, +; Wassermann, —	Clinical diagnosis: (1) acute rheumatic polyarthritis; (2) later, uremia, terminal pneumonia Necropsy: periarteritis nodosa; macroscopic, nodules on coronary arteries; thickening of walls of larger kidney vessels seen on cross section with narrowing of lumen; contracted kidneys with anemic infarct; microscopic, periarteritis nodosa of arteries of kidneys, in coronary arteries and heart muscle; terminal diffuse, confluent bronchopneumonia
±	..	..	+ Punctate hemorrhages over body	..	....	Sudden onset with vomiting and abdominal pain 2 wks. prior to admission; persistence of abdominal pain; diarrhea in 3d wk.; sudden collapse with increasing pallor, finally pulseless, death	Clinical diagnosis: not given but apparently considered some type of colitis Necropsy: periarteritis nodosa; macroscopic, nodules on vessels of pericardium, stomach and small intestines; peritoneal hemorrhage, 1,500 cc.; blood in abdominal cavity, from aneurysmal rupture of capsule on the outer margin of the liver and from laceration of the liver; internal hemorrhage cause of death; microscopic, periarteritis nodosa of pericardium, liver, kidneys and intestinal wall
+++	..	..	On 10th day: hemorrhagic mucocutaneous papules and bullae; ecchymotic plaques; hemorrhagic lesions become necrotic and ulcerative	..	+	Sudden onset with severe abdominal pain and pain in extremities; profuse, progressive diarrhea	Clinical diagnosis: (1) at first, rheumatism; (2) later, undiagnosed save for acute glomerulonephritis Necropsy: periarteritis nodosa; macroscopic, nodules in intestines and spleen; microscopic, involvement of intestines, kidneys and spleen

TABLE 3.—*Data on Cases*

Author and Year	Age of Child, Sex	Duration of Illness	Pulse Rate	Temperature	Blood Pressure	Red Blood Cells	White Blood Cells	Urine
Hutinel and co-workers, 1930	10 yrs. ♀	2 wks.	130	38.2 C.	..	.....	Total count not given but polymorphonuclears, 92%	0
Damblé, 1930	7 yrs. ♀	1½ mos.	On admission: 118 to 125	38 C. to 39.1 C.	120/40	2,140,000 with hemoglobin, 35%	17,400, with polymorphonuclears, 66% (segment, 19%; stab, 47%); lymphocytes, 30%; eosinophils, 3%; monocytes, 1%	Albumin, 0; R.B.C., casts and W.B.C. present Later: Albumin, +
			Day prior to death: 120	38.5 C.	130/75			
Herlitz (second case), 1930	12 yrs. ♀	3 wks.	80 to 100	38 C. to 39 C.	..	3,410,000 with hemoglobin, 70%	28,800, with polymorphonuclears, 92%; monocytes, 8%	Albumin, +; W.B.C., large clumps; R.B.C., few; casts, 0
Lindberg, 1931	15 yrs. ♀	4½ yrs.	100 to 120	a.m. 36.6-37 C.; p.m. 37.5-38 C.	During illness 90/60	3,490,000 with hemoglobin, 55%; sedimentation rate, 95 mm. per hr.	15,900, with polymorphonuclears, 71%; lymphocytes, 21.5%; eosinophils, 2.5%; monocytes, 5%	0 Albumin, 0; sediment, negative
					At time of report of case (after symptom-free for 2 mos.): 95/70	Hemoglobin, 70%; sedimentation rate, 10 mm. per hr.		
Case 1 of present report, 1928 and 1932	10 yrs. ♂	6 mos.	124 to 78	Range: 98.6 F. to 103 F. Peak: 103 F.	Last 2 mos.: 145/112 increased to 176/138	4,000,000 with hemoglobin, 92%	11,000, with polymorphonuclears, 80%; lymphocytes, 15%; monocytes, 4%; eosinophils, 1%	0 Occasional faint traces of albumin
			(Tentatively diagnosed periarteritis nodosa) child presented 1 month prior to death at subsequently, case reported at meeting of New York Pathological Society by Dr.					
Case 2 of present report, 1932	7 yrs. ♂	9 wks.	124	Range: 100 to 103 F. Peak: 103 F.	..	On admission: 5,000,000 with hemoglobin, 70% Two days prior to death: 2,500,000 with hemoglobin, 38%	16,000, with polymorphonuclears, 81%; lymphocytes, 17%; monocytes, 2%	0 Throughout illness

Abdominal Pain	Liver	Spleen	Skin Manifestations	Sore Throat	Arthritis	Addenda	Clinical Diagnosis vs. Necropsy
++	0	0	On 4th day: scarlatiniform rash; on 6th day: purpuric rash; on 7th-9th days: necrotic ulcerations	0	++	Sudden onset with malaise, increasing weakness; abdominal pain and joint pains; bloody diarrhea	Clinical diagnosis: (1) at first, typhoid fever; (2) then rheumatic purpura or sepsis; (3) on tenth day, clinical diagnosis of periarteritis nodosa (Reilly) Necropsy: periarteritis nodosa; macroscopic, nodules on intestines; microscopic, involvement of intestines, spleen and skin arteries
....	+	..	0	0	0	Eyegrounds, normal; rising blood pressure; increasing edema; drowsiness with convulsions; coma with death	Clinical diagnosis: acute glomerulonephritis with uremia Necropsy: Periarteritis nodosa of kidneys, gallbladder, liver heart, lung and spleen
....	..	..	Bluish-red hemorrhagic blotches on hands	+	..	On 14th day, paralysis of right arm; lumbar puncture, fluid negative; terminal phalanx of left thumb and little finger became bluish, cold and slightly painful	Clinical diagnosis: septicemia Necropsy: periarteritis nodosa; macroscopic, nodules on coronary arteries; infarcts of ventricle; microscopic, periarteritis nodosa of heart, kidneys, spleen, vessels of left little finger and vessels along nerves of right bronchial plexus
0	0	+	Recurrent crops of small, tender, reddened, subcutaneous nodules on legs, arms and trunk	0	+	Onset 4 yrs. prior to present attack; had experienced two previous attacks, each lasting 1 mo., within an interval of 4 mos., similar in all respects to present attack; present illness lasted for 6 mos., characterized by weakness, emaciation, subfebrile temperature, rapid sedimentation rate, pains in joints and muscles of legs, disproportionately high pulse rate, multiple crops of subcutaneous nodules	Clinical diagnosis: "in vivo" diagnosis of periarteritis nodosa (made 3 mos. after onset of present attack) based on histologic examination of a subcutanous nodule removed at biopsy; child had been free of symptoms with no evidence of continuation of the disease process during the 2 mos. period prior to the writing of Lindberg's report
0	+	0	0	0	0	Pain in muscles of both upper and lower extremities leading to atrophy of muscles with resultant contractures; Wassermann negative during last 2 mos. of life, repeated convulsions with loss of consciousness; vastly deteriorated sensorium; acute orchitis; death from terminal pneumonia; "in vivo" tentative diagnosis of periarteritis nodosa based on histologic examination of muscle biopsy	Clinical diagnosis: (1) at first, polymyositis or trichinosis; biopsy on piece of muscle from right artery on histologic examination revealed dilatation of vessels with definite perivascular infiltration of polymorphonuclears (done 4 mos. prior to death); (2) "in vivo" tentative diagnosis of periarteritis nodosa (after biopsy report) Necropsy: macroscopic, nodules on coronary arteries and on branches of hepatic artery; one nodule on stomach; microscopic, periarteritis nodosa of heart, liver, pancreas, suprarenal, stomach, small intestines, hepatic artery, renal arterial branches, intrahepatic
Mount Sinai Clinical Conference, February, 1924; Welt							
+	+	0	Edema, +	0	....	Scarlet fever 2 mos. prior to admission; desquamated, then in third week had cervical adenitis; abdominal pain after adenitis; then pain in foot, thumb, groin and scrotum (4th, 5th, 6th wk.); gradual development of pallor, weakness, cyanosis, edema, with cardiac decompensation; death	Clinical diagnosis: Acute rheumatic cardiovalvular disease with progressive cardiac decompensation Necropsy: both periarteritis nodosa and rheumatic endocarditis; macroscopic, nodules throughout lungs and on right coronary artery, verrucous vegetations on posterior flap of mitral valve; microscopic, (1) periarteritis nodosa involving lungs, kidneys, coronary arteries and external iliac artery; (2) rheumatic endocarditis with typical Aschoff bodies in heart

TABLE 4.—*Analysis of Cases in Children* *

Author	Age	Sex	Duration of Illness	Previous Illnesses	Onset	Increased Pulse Rate	Fever	Elevated Blood Pressure	Anemia	Leukocytosis	Weakness	Vomiting	Urine: Albumin	Urine: Casts	Urine: Red Blood Cells	Urine: White Blood Cells	Liver	Spleen	Abdominal Pain	Sore Throat	Muscle Pain or Joint Pain	Subcutaneous Nodules	Other Skin Manifestations	Edema	Headache	Convulsions	Coma
Kundrat.....	10 yrs.	♀	..	.....	.....	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	.....	..	..	..	..
Krzyszkowski	2½ mos.	..	11 days	.....	.....	..	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	Indefinite rash	+	..	..	..
Vesprémi and Janscó	14 yrs.	♂	6 mos.	.....	.....	..	+	..	..	..	..	..	+	+	—	—	..	..	..	..	..	..	Urticaria; petechiae	+	..	+	+
Dickson.....	14½ yrs.	♂	10 wks.	.....	Subacute	..	+	..	..	..	+	+	..	..	..	..	..	..	..	..	..	..	.....	..	+	+	+
Vesprémi (second case)	10 yrs.	♂	3 wks.	.....	Acute	..	..	..	..	..	+	+	..	..	..	..	..	..	..	..	..	..	Rash	+	+	+	+
Lamb (second case)	10 yrs.	♀	5-6 wks.	Measles; diphtheria	Acute	+	+	+	..	+	..	+	+	+	—	—	..	..	++	++	+	..	Mottled erythema	+	..	..	..
Pickert-Menke	13 yrs.	♂	9-10 wks.	Measles; scarlet fever	Subacute	..	+	..	+	+	+	..	..	..	..	..	..	..	++	..	+	..	.....	+++	..	+	±
Lemke (first case)	11 yrs.	♂	6 wks.	Grip at onset	Subacute	+	+	..	..	..	..	+	..	..	..	..	..	..	+	+	..	..	.....	..	..	..	..
Lemke (third case)	5 yrs.	♂	4 wks.	Sore throat at onset	Subacute	..	..	+	..	..	..	..	+	+	+	—	..	..	+	++	..	..	.....	+	..	+	+
Wordley.....	13 yrs.	♂	8 wks.	.....	Acute	+	+	+	..	+	..	..	+	+	+	+	..	..	++	..	..	..	.....	..	..	++	±
Gruber.....	14 yrs.	♂	7-8 wks.	Measles; tonsillitis; onset with tonsillitis	Subacute	+	+	+	+	+	..	..	+	+	+	+	..	..	+	+	..	..	.....	+	..	+	+
Thinnes.....	9 mos.	..	4 hrs.	Measles ?	Acute	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	..	..	.....	..	..	..	..
Gray.....	12 yrs.	♂	9 wks.	Infection of thigh at onset	Acute	+	+	..	..	..	+	..	..	..	..	..	..	..	..	..	++	..	Redness and swelling locally	..	..	..	..
Kimmelstiel....	10 yrs.	♀	3½ Mos.	Pertussis; measles; cervical adenitis; acute otitis at onset	Acute	..	+	..	..	+	..	+	..	..	..	..	..	..	+	..	..	..	.....	..	..	+	..
Basch.....	13 yrs.	♀	4 mos.	Measles; pertussis; chickenpox; sore throat; onset with grip	Subacute	..	+	+	+	+	..	..	+	+	—	+	..	+	..	..	+	..	Rash	..	..	+	+
Baló and Nächtnebel	14 yrs.	♂	5 wks.	Pertussis; measles	Acute	..	..	..	..	..	+	+	..	..	..	..	..	..	+ (severe diarrhea)	..	..	..	Punctate hemorrhages	..	..	..	..
Debré and coworkers	3 yrs.	♂	2 wks.	Measles; colitis	Acute	+	+	..	..	..	+	+	+	+	+	+	..	..	+ (severe diarrhea)	..	+	..	Mucocutaneous hemorrhages with ulcerations	..	+	..	..
Hutinel and coworkers	10 yrs.	♀	2 wks.	Measles; tuberculous contact	Acute	+	+	..	..	+	+	..	..	..	..	..	..	..	++ (bloody diarrhea)	..	++	..	Scarlatiniform, then purpuric	..	..	..	..
Damblé.....	7 yrs.	♀	1½ mos.	.....	Acute	+	+	+	+	+	+	..	—	+	+	+	+	..	..	..	..	..	.....	+	..	+	+
Herlitz.....	12 yrs.	♀	3 wks.	Measles; mumps; onset with acute sore throat	Acute	+	+	..	+	+	..	..	+	—	+	+	..	..	..	+	Paralysis of right arm; embolic phenomena of fingers	..	Blotchy hemorrhagic rash	..	..	..	..
Lindberg.....	15 yrs.	♀	4½ yrs.	Measles; tuberculous contact	Chronic with acute exacerbations	+	0	0	+	+	+	..	..	..	..	..	..	+	..	..	+	++	.....	..	..	..	..
Present report, case 1	10 yrs.	♂	6 mos.	.....	Subacute	+	+	+	+	+	+	..	—	—	—	—	..	+	..	..	+	..	.....	..	..	+	+
Present report, case 2	7 yrs.	♂	9 wks.	Pertussis; mumps; measles; chickenpox; onset following scarlet fever	Acute	+	+	..	+	+	+	+	—	—	—	—	+	..	+	..	+	..	.....	..	+	..	..

TABLE 4.—*Analysis of Cases in Children* *—Continued

Author	Clinical Type of Death	Periarteritis Nodosa	Organs Found Involved by Periarteritis Nodosa at Necropsy
Kundrat.....			
Krzyszkowski			
Vesprémi and Janscó			
Dickson.....			
Vesprémi (second case)			
Lamb (second case)			
Pickert-Menke			
Lemke (first case)			
Lemke (third case)			
Wordley.....			
Gruber.....			
Thinnes.....			
Gray.....			
Kimmelstiel....			
Basch.....			
Baló and Nächtnebel			
Debré and coworkers			
Hutinel and coworkers			
Damblé.....			
Herlitz.....			
Lindberg.....			
Present report, case 1			
Present report, case 2			

following scarlet fever

TABLE 4.—*Analysis of Cases in Children*—Continued*

Author	Clinical Type of Death: Cardiac Insufficiency	Clinical Type of Death: Renal Insufficiency, Uremia	Clinical Type of Death: Cerebral Hemorrhage or Meningitis	Clinical Type of Death: Peritoneal Hemorrhage	Clinical Type of Death: Other Types	Clinical Diagnosis	Periarteritis Nodosa Found on: Macroscopic plus Microscopic	Periarteritis Nodosa Found on: Microscopic Only	Organs Found Involved by Periarteritis Nodosa at Necropsy: Kidneys	Heart	Coronary Artery	Lungs	Liver	Pancreas	Spleen	Adrenals	Stomach	Intestines	Cerebral Vessels	Other Organs	Addenda
Kundrat	..	..	..	..	....	Marasmus ?	+	..	..	+	++	..	..	..	..	..	..	..	..	.....	
Krzyszkowski	..	..	..	..	....	Syphilis ?; scarlet fever ?	+	..	..	..	++	..	..	..	..	..	..	..	..	.....	Hemorrhagic nephritis; bronchopneumonia
Véprémi and Jancsó	..	..	+	..	....	Meningitis ?; cerebral hemorrhage ?	+	..	..	+	++	..	..	..	..	..	+	+	+	.....	Meningeal hemorrhage
Dickson	..	..	+	..	....	Tuberculosis or pneumococcal meningitis	+	..	+	+	++	..	+	..	+	..	..	..	++	.....	Cerebral hemorrhage
Vesprémi (second case)	..	+	..	..	....	Acute glomerulonephritis	+	..	..	+	..	..	..	..	..	..	+	+	..	Urinary bladder +	Glomerulonephritis
Lamb (second case)	..	..	..	..	Sepsis?	Acute appendicitis (appendectomy); acute tonsillitis with secondary nephritis and polyarthritis	+	..	+	+	+	..	+	+	+	..	..	..	..	Bronchial arteries +	
Pickert-Menke	+	..	..	..	....	Pus in left kidney (puncture unsuccessful); muscular atrophy or neuritis	+	..	+	+	+	+	+	+	+	..	..	+	..	.....	
Lemke (first case)	..	..	..	+	....	Acute surgical abdominal condition (laparotomy done); sudden collapse with death 4 weeks postoperatively	+	..	+	+	+	..	+	..	..	+	..	..	..	.....	Peritoneal hemorrhage from ruptured liver aneurysm
Lemke (third case)	..	+	..	..	....	Acute nephritis with uremia	0	+	+	.. (Only right kidney removed for examination)										.....	Glomerulonephritis
Wordley	..	+	..	..	....	Renal calculus; renal neoplasm	+	..	+	.. (Only heart and kidneys examined Microscopically)		+									
Gruber	..	+	..	..	....	Acute nephritis secondary to sore throat; tonsillar abscesses with secondary sepsis	0	+	.. (The only organs examined microscopically were liver and gallbladder)				+	..	..	..	..	..	..	Gallbladder +	
Thinnes	..	..	..	..	?	Acute pharyngitis	+	..	+	+	..	..	..	..	..	..	..	..	..	.....	Kidney infarcts
Gray	..	..	..	+	....	Cellulitis of thigh with inguinal adenitis; sudden collapse with death 9 weeks after onset	+	..	+	..	+	..	+	..	..	..	..	..	..	.....	Peritoneal hemorrhage from ruptured aneurysm of cystic artery
Kimmelstiel	..	..	+	..	....	Acute appendicitis (laparotomy done); ? cerebral hemorrhage 3 months postoperatively	+	..	+	+	..	..	..	+	+	..	+	+	+	+ gallbladder; peripheral nerves; uterus ovaries; bladder	Cerebral hemorrhage from rupture of undiscovered aneurysm of cerebral artery
Basch	..	+	..	..	Pneumonia	Rheumatic polyarthritis	+	..	+	+	+	..	..	..	..	..	..	..	..	.....	Bronchopneumonia; tuberculous primary focus in right upper lobe (subpleural)
Baló and Nächtnebel	..	..	..	+	....	Not given; sudden collapse with death 4 weeks after onset	+	..	+	Vessels of pericardium			+	..	..	..	..	+	+	.....	Peritoneal hemorrhage from ruptured liver aneurysm
Debré and co-workers	..	+	..	..	Sepsis ?	Rheumatism; acute glomerulonephritis	+	..	+	..	..	..	..	..	+	..	..	+	..	.....	
Hutinel and co-workers	..	..	..	..	Sepsis	Typhoid fever ?; rheumatic purpura or sepsis ?; periarteritis nodosa (Reilly)	+	..	..	..	..	..	..	..	+	..	..	+	..	+ arteries of skin	
Damblé	..	+	..	..	....	Acute glomerulonephritis with uremia	0	+	+	+	..	+	+	..	+	..	..	..	..	+ gallbladder	
Herlitz	..	..	..	..	Sepsis	Septicemia	+	..	+	+	+	..	..	..	+	..	..	..	..	+ vessels of left little finger; vessels to right brachial plexus	
Lindberg	(Patient living)					Periarteritis nodosa (in vivo)	Biopsy of subcutaneous nodule showed periarteritis nodosa														
Present report, case 1	..	..	+	..	....	Polymyositis of trichiniasis ?; periarteritis nodosa (in vivo)	+	..	+	+	+	..	+	+	..	+	+	..	..	+ muscle tissue; + mesenteric artery and + hepatic artery (biopsy of muscle tissue showed periarteritis nodosa)	
Present report, case 2	+	..	..	..	....	Rheumatic cardiovalvular disease with decompensation	+	..	+	.. Heart showed Aschoff bodies; verrucous rheumatic vegetations on mitral valve		+	+	+	+	+	+	..	..	+ external iliac artery	

* Tabulation of symtomatology, clinical findings and organic involvement at necropsy; only positive data are charted, for the cases are not completely described in the literature.

in general. The duration of the symptoms of the disease has been given in 22 of our cases and varied from four hours (Thinnes) to four and one-half years (Lindberg). Thus, in 5 cases, the duration of illness was less than one month; in 5 cases, between one and two months; in 5 cases between two and three months; in 3 cases, four months; in 2 cases, six months; and in only 1 case, longer than six months—four and one-half years.

In attempting to evaluate the symptoms, physical findings or necropsy observations, we can enumerate only the number of cases in which any one factor has been present for several of the reports are very brief and incomplete, and in others a particular individual symptom or finding may not be referred to. The course appears to have been moderately acute in all cases save for that of Lindberg. Increased pulse rate was noted in 12 cases; fever in 17 cases and absent in only 2 cases; an elevated blood pressure in 7 cases; anemia in 8 cases; leukocytosis in 12 cases; weakness apparently sufficiently extreme to have been specifically mentioned in 11 cases; vomiting in 8 cases; urinary findings in 9 cases, in 6 of which urinalysis showed red blood cells and in 7, casts; the liver palpably enlarged in 2 instances; the spleen enlarged in 3; abdominal pain of varying severity in 12 cases, in 3 of which laparotomy was mistakenly performed for an acute surgical condition of the abdomen; sore throat in 6 cases; muscle or joint pain in 9 cases; skin rashes in 8 cases, in 5 of which the rash was hemorrhagic or petechial in character; edema in 8 cases, either localized or generalized; subcutaneous nodules in only 1 case (Lindberg); headache in 4 cases; convulsions in 11 cases followed by coma in 9 cases; diarrhea in 3 cases, in 1 of which gross intestinal bleeding was present (Hutinel).

Clinically, death in the 20 cases seemed to be secondary to cardiac insufficiency in 2 cases, to renal insufficiency with uremia in 7 cases, to cerebral hemorrhage or meningeal involvement in 4 cases, to internal or peritoneal hemorrhage in 3 cases and to some form of sepsis in 3 cases. In 1 case (Thinnes), the cause of death was not clear. Only 1 case (Lindberg) went on to an apparent cure. The clinical diagnoses varied—laparotomy was performed for acute surgical conditions in 3 cases (Lamb, Lemke's first case, Kimmelstiel); in 1 case (Pickert-Menke), pus in the left kidney was suspected but puncture was unsuccessful; meningitis was suspected in 2 cases, cerebral hemorrhage in 2 cases, nephritis in 6 cases, renal calculus or neoplasm in 1 case, rheumatic fever or its complications (polyarthritis, purpura or cardiovalvular disease) in 5 cases, muscular atrophy or neuritis in 1 case, syphilis in 1 case, typhoid fever in 1 case, sepsis in 5 cases; polymyositis or trichiniasis in 1 case. Periarteritis nodosa was diagnosed in vivo based in 1 case (Lindberg) on a biopsy of a subcutaneous nodule and

in another (our first) on histologic examination for possible trichiniasis of a piece of muscle tissue removed at biopsy. In 1 case (Hutinel), the diagnosis was made in vivo by Reilly unsupported by any histologic evidence during life but later confirmed at necropsy.

At necropsy, in 3 cases (Lemke's third case, Gruber, Damblé), evidence of periarteritis nodosa was not observed macroscopically, and the diagnosis was made only after careful microscopic study. In several of the cases, the necropsy was incomplete, for only individual organs were examined (Kundrat, heart; Lemke, right kidney; Wordley, only heart and kidneys examined microscopically; Gruber, only the gallbladder and liver examined microscopically). In other cases, complete details indicating whether or not various organs have been involved are lacking However, such records as do exist reveal the individual organs to have been involved as follows: kidneys, 16 times; heart, 13; coronary arteries, 13; lungs, 3; liver, 10; pancreas, 5; spleen, 9; suprarenals, 3; stomach, 6; intestine, 7; cerebral vessels, 3; gallbladder, 3; urinary bladder, 2; uterus and ovaries, 1; vessels to peripheral nerves, 2.

SUMMARY AND CONCLUSION

1. Periarteritis nodosa should be considered in every case of acute or chronic sepsis with sterile blood cultures and a bizarre symptomatology unexplainable on a common basis, particularly if associated with a severe anemia, a febrile course, gastro-intestinal symptoms, joint, muscle or skin manifestations and signs of renal involvement together with an elevated blood pressure.

2. In such cases careful examination should be made each day for possible subcutaneous nodules. If these are present, a biopsy should be done.

3. Negative gross findings at necropsy cannot rule out the possible presence of periarteritis nodosa, for in a significant number of cases the pathologic changes can be demonstrated only after a careful microscopic examination of every organ. The disease process may be sufficiently widespread to involve several organs, but at times it may be localized to one organ, and even that organ may be involved only by microscopic changes. The importance of a complete routine microscopic examination cannot be too greatly emphasized.

4. Two cases of periarteritis nodosa occurring in boys of 10 and 7 years of age, respectively, are reported in this paper with complete case histories and necropsy observations. In the first child presented, a tentative diagnosis was made in vivo one month prior to death based on the bizarre symptomatology and the suggestive findings on histologic examination of a piece of muscle tissue removed at biopsy. In the second case, periarteritis nodosa and rheumatic cardiovalvular disease were found coexistent at necropsy.

5. Twenty-one additional cases of periarteritis nodosa occurring during infancy and childhood (in persons under 15 years of age) have been found in the literature, and an abstract of each case has been appended (table 3).

6. In a total of 195 proved cases of periarteritis nodosa, the disease occurred 23 times (including our own 2 instances) during infancy and childhood, or a percentage of 11.8.

7. In our opinion, the diseases now classified under the name of "periarteritis nodosa" are similar syndromes or symptom complexes which are probably caused by a variety of infectious agents. Thus far, a specific etiologic factor has not been proved, and the theory that the initial pathologic changes represent an allergic response on the part of the blood vessels to the noxa responsible for the disease remains speculative.

8. The name "periarteritis nodosa" when applied to the entire group of cases is a misnomer. The term "nodosa" is apt to be misleading to those unacquainted with the disease, for in only a comparatively small proportion of the cases are subcutaneous nodules observed (12.5 per cent according to Herlitz), and in a number of the cases on record there have been no gross nodules or thickenings in the vessels at necropsy, and the disease process has been recognized only on thorough microscopic examination. We would suggest that the term "periarteritis," subdivided into acute, subacute or chronic stages, might be a more appropriate name for the entire group of cases until such a time as the discovery of the etiologic factors enables us to designate the component parts of this group of disease processes more fittingly.

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Pediatric Biographies

JOSEPH RAULIN

1708-1784

JOHN RUHRÄH, M.D.

BALTIMORE

Joseph Raulin was born in 1708 at Aiguetinte, and after receiving his doctor's degree he practiced first at Nérac, in Gasgony, where his talents showed themselves to be worthy of a wider field; so he removed to Paris. Little is recorded concerning his life, but he was a "joiner" and a member of many learned societies, not only of France but also of Italy and of England. He was a medical councilor-in-ordinary to the King and a royal censor. He was a prolific writer, and over a dozen treatises exist to prove his industry. The treatises cover all sorts of subjects, from tapeworm to the properties and uses of mineral waters and the use of coal as a fertilizer. He also wrote on gynecology and children, and his book on the latter subject is best known. He wrote two works on disturbances caused by variations in the air and by dry heat, cold and humidity. It is entitled "De la conservation des enfans, ou, les moyens de les fortifier, de les préserver et guerir des maladies depuis l'instant de leur existence, jusqu'a l'âge de puberté. The first volume appeared in two parts in Paris in 1768, and the second volume followed in 1769. It was intended to complete the work, which was undertaken by order of Louis XV, in eight volumes.

The book has a preliminary discourse, and then with a thoroughness almost teutonic, starts with a subject dear to the gallic heart, the generation of the child, which together with what is said about pregnancy, takes up the entire first part, while the fetus, its diseases and malformations fill the second part. So, as in "Tristram Shandy," one does not get to the born child until one is over half way through the book. The part of the work called the second epoch fills the remainder. This part takes one only up to the weaning period, and is devoted to the care necessary to infants, how to nourish them and how to treat their diseases.

The first ten pages are devoted to tying the cord, to feebleness in the new-born infant, to the skin and its proper cleansing; ten more pages take up the subject of bathing. There is a chapter on the variants of the foregoing material and another of reflections on the same sub-

ject, the examination of the new-born, the binder and the meconium. The second section deals with the feeding by nursing and by using the milk of animals.

One small extract must serve as an example of the author's style and method of presentation.

DE LA

CONSERVATION

DES ENFANS,

Ou les moyens de les fortifier, de les préſerver & guérir des maladies, depuis l'inſtant de leur exiſtence, juſqu'à l'âge de puberté.

Par M. RAULIN, Docteur en Médecine, Conſeiller Médecin ordinaire du Roi, Cenſeur Royal, de la Société Royale de Londres; des Académies des Belles-Lettres, Sciences & Arts, de Bordeaux & de Rouen, & de celle des Arcades de Rome.

TOME PREMIER.

Spes gentis & robur.

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Title page of Raulin's book.

THE NOURISHMENT OF INFANTS WITHOUT RECOURSE TO MILK

As milk which is natural to infants and that which is foreign to them are susceptible of acquiring qualities contrary to their nourishment and of causing diseases, often even death; the wise nations and those of enlightened men have tried to supplement it by other means. Ferrarius teaches us that the Germans, frightened at this danger, have no difficulty in nourishing their children from their birth with pap composed of the milk of cows or sheep and of barley flour. It is the country which still today uses this method and it is much employed in Upper Germany and in Switzerland and even in France. They give the child this nourishment every four hours and make it drink between times. The most healthy drink, which these people serve is water in which they boil the raspings

of a deer horn or ivory and anise seeds. When the ordinary pap seems to incommode the children on account of its sourness and glutinosity, it is replaced by meat juice, the yelk of egg and bread or with toast reduced to powder and mixed with milk or meat juice. In the second year they give more solid foods. In Basel they feed the foundlings a pap made of milk and flour; water is their only drink. It is not noticed that children so fed die any more than those brought up differently, nor are their diseases any more frequent or more dangerous in one than the other. Van Helmont feared to nourish children with milk on account of acquiring conditions which are harmful. This author thinks his belief is justly founded and advises to nourish infants from their birth, in place of milk, on a pap made of bread boiled in small beer, which he sweetens with sugar or honey and reduces to a jelly. This he mixes with a little small beer to make a drink for the children. He gives first very light food and then after they are accustomed to that, more solid things. It is thus this author has nourished many infants from their birth and principally the son of a count, who became larger, stronger and more courageous than his brothers. This young man gave great promise, but had the misfortune to receive, in the army, a bullet which ended his days. Van Helmont places this pap above other foods for feeding babies. One can see in his books praise which perhaps he overstates.

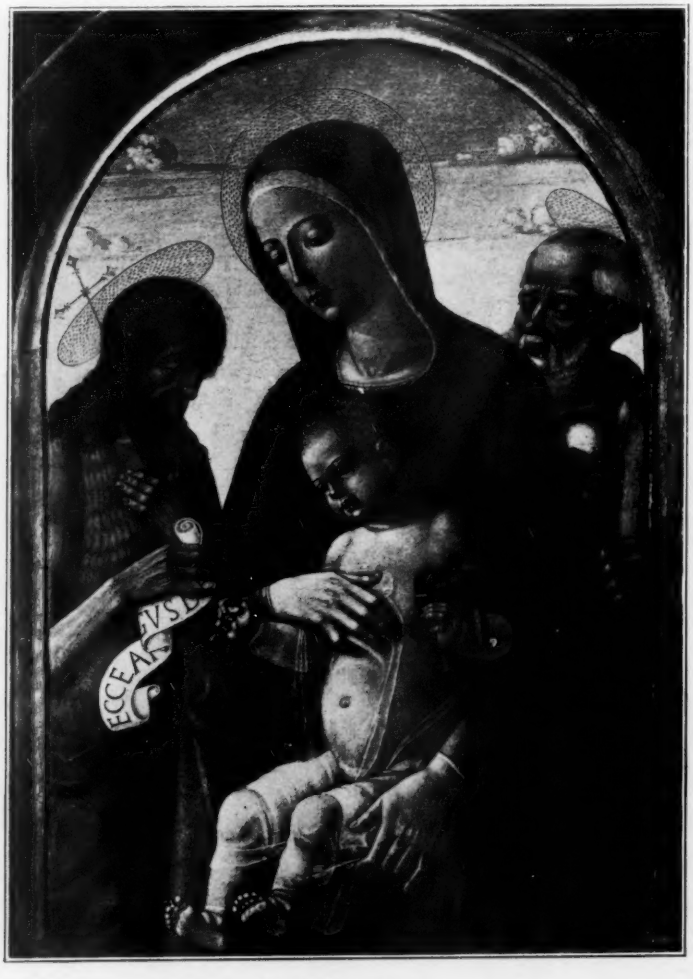
One is surprised at this proposal of a beer pap; nevertheless this usage is not without example, and one sees it in Holland and Denmark. In one and the other it is made ordinarily with milk, but often with beer in place of milk as Van Helmont suggests. There is little difference between the paps made with beer and those made with water, as the volatile part of the beer is dissipated by the boiling and there rests in the pap only the aqueous part, so there is little to choose as it is equivalent to ordinary water. This author dilutes the pap with beer to make an ordinary drink for infants. I do not agree with the healthfulness of this usage. It would be dangerous in our climate.

Pediatrics in Art

PITUITARY DISTURBANCES: GIGANTISM

JOHN RUHRÄH, M.D.
BALTIMORE

An unknown master of the Siena school painted a picture of the Holy Family which now hangs in the picture gallery in Dresden. In this the child shows unmistakable evidences of pituitary disturbance as is evidenced by the considerable overgrowth. The tendency to gigantism is very apparent. There are a number of art works which show endocrine disturbances, but few of this type. The photograph is by F. Bruckman of Munich.



The Holy Family.

News and Comment

GENERAL

Columbia University Medal Awarded to Dr. Chapin.—At the commencement exercises at Columbia University on June 6, President Butler presented to Dr. Henry Dwight Chapin the university medal for excellence awarded in recognition of his outstanding contribution to problems relating to the care of children.

Lectures in Pediatrics.—During the summer and fall a one day lecture course in pediatrics will be conducted in eleven districts of Illinois, under the auspices of the American Academy of Pediatrics and the educational committee of the Illinois State Medical Society. The following cities have been tentatively selected as the centers: Chicago, Rockford, Rock Island, La Salle, Peoria, Springfield, Quincy, Champaign, East St. Louis, Effingham and Benton. Subjects to be covered by the course include care of the new-born, care and feeding of infants, preventive pediatrics, behavior problems and discipline in children, and general treatment of the sick child. The five pediatricians who have been selected to organize groups of teachers are Drs. Isaac A. Abt, Julius H. Hess, Joseph Brennemann, Clifford G. Grulee and Robert A. Black, all of Chicago.

DEATHS

Prof. Dr. Leopold Moll died unexpectedly, in the midst of his work, at the age of 56. Born in Prague, he attended the university in that city and was called by Professor Ebstein to serve as assistant in the Säuglingsklinik. In 1909 he was summoned to Vienna by Professor Escherich, where he organized the Reichs-Anstalt für Mütter- und Säuglingsfürsorge. By the admission of both mother and child, Professor Moll promoted the idea of breast-feeding. He disseminated the knowledge of infant feeding among physicians, nurses and the public. From all directions, physicians came to this institute. Medicine is indebted to him for the creation of numerous consultation centers for mothers and for prenatal care. The organization of the movement to provide after-care for convalescent children was his work, and more than 25,000 children are indebted to this institution for the recovery of health. Among his more important scientific publications may be mentioned studies on the various foods for infants, the pathology and treatment of pyloric spasm and the relation of climate to diseases of children.

On February 23 Jean Hutinel died rather suddenly. As recorded in *The Journal*, he was the son of Victor Hutinel. On March 21, less than one month after the death of his son, Victor Hutinel, who has meant so much to French pediatrics, died. He was one of the most respected of the French physicians. He was born in 1849 and was a student of Parrot's. To record his various activities is impossible and would not in any way add to the respect which everybody held for him. The sadness of his going one month after the death of his most promising son adds pathos to tragedy. We extend our sympathies to the French pediatric profession.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

FUNCTION OF THE FETAL SPLEEN IN SPLENECTOMIZED PREGNANT RATS. A. BERGER and E. FLAUM, Ztschr. f. d. ges. exper. Med. **80**:531, 1932.

In splenectomized pregnant rats which have been infected with Bartonella there appears evidence of anemia with marked blood regeneration: Howell-Jolly bodies in the erythrocytes, megaloblasts, nucleated red blood cells and polychromasia. These changes appear from two to five days after splenectomy and do not occur in normal animals or in pregnant rats from which the spleens have not been removed. The conclusion is drawn that the fetal spleen is unable to take over the function of the maternal spleen in the splenectomized rat.

COHEN. [ARCH. PATH.]

DETERMINATION OF UROBILIN (SCHLESINGER). G. C. E. BURGER and B. H. STOCKMANN, Nederl. tijdschr. v. geneesk. **76**:1369 (March 19) 1932.

The great importance of urobilinuria makes it necessary to have a simple, rapid and practicable quantitative method of determining the urobilin in the urine. A colorimetric method is described, which is founded on the determination of the intensity of the fluorescence in the reaction of Schlesinger. The green fluorescence of the reaction is compared with that of a watery solution of acriflavine.

For the determination of a pathologic urobilinuria one has to examine in many cases also the morning urine in view of the nature of the physiologic secretion of urobilin. To obtain the reaction of Schlesinger one must make the urine faintly alkaline to litmus, and use a freshly prepared suspension of zinc acetate or absolute alcohol.

VAN CREVELD, Amsterdam, Holland.

MECHANISM OF COAGULATION OF THE BLOOD. L. J. DEL BAERE, Nederl. tijdschr. v. geneesk. **76**:1377 (March 19) 1932.

Of the many theories as to the mechanism of coagulation of the blood, only one enters into the colloidochemical significance of the phenomenon. This is the hypothesis of Mills, which is not yet proved or worked out. The author therefore made an extensive study of the colloidochemical side of the problem and came to the following conclusions:

1. With the help of cataphoresis, the author shows how thrombin is positively charged, whereas prothrombin is negatively charged, as are all other plasma colloids.

2. For that reason the author looks on the formation of fibrin as a kind of precipitation of colloids: a precipitation of the negatively charged fibrinogen and the positively charged thrombin.

3. With the help of colloido-osmotic measures he shows that although precipitation does not appear when mixing thrombin and serum albumins, a coupling of these two substances must arise. This the author established by a fall of the colloido-osmotic pressure of the serum during the first few hours after the coagulation, and by the disappearance of part of the active thrombin (formation of metathrombin).

4. Mentioning the experiments of Bungenberg de Jong, he points out how, without the production of new thrombin, more free thrombin can be present after coagulation than before.

5. The author raises the hypothesis that in vivo there is a continual formation of thrombin, and that this thrombin is absorbed by the negatively charged vessel wall, where it is reduced by heparin to the original prothrombin.

VAN CREVELD, Amsterdam, Holland.

RESPIRATION IN CHILDHOOD. M. DE BRUIN, Nederl. tijdschr. v. geneesk. **76:** 1466 (March 26) 1932.

The study of a large number of respiration curves (by means of Krogh's spirometer) as to the frequency and depth of respiration and the absolute respiration volume, in fifty-one children ranging in age from 1½ to 10 years, showed that as a rule frequency and depth of respiration did not differ much in the same child on two successive days. With increasing age no pronounced decrease in frequency of respiration was observed.

Some children showed marked differences from the normal, in both frequency and depth of respiration. A few showed great fluctuations on succeeding days. In such cases a high frequency was often found with an increased depth of respiration; this was clearly evident from the great differences in the absolute respiration volume. There existed no close relation between high basal metabolism and increased absolute respiration volume.

VAN CREVELD, Amsterdam, Holland.

RAPID AND SIMPLE DETERMINATION OF THE BLOOD SUGAR. A. J. L. TERWEN, Nederl. tijdschr. v. geneesk. **76:**2487 (May 21) 1932.

An account is herewith given of a rapid and simple method of determining blood sugar. This method is based on the reduction with alkali of potassium ferricyanide to potassium ferrocyanide; this is converted into prussian blue by the addition of a ferric salt. The prussian blue, kept in solution by pyrophosphoric acid, is colorimetrically determined by comparison with a solution obtained in the same way from a solution of dextrose of 1 Gm. per liter. The colors of the two final solutions are then compared and made the same by diluting the stronger with a weak solution of potassium ferricyanide. The ratio of concentrations of dextrose is calculated from the degree of concentration.

VAN CREVELD, Amsterdam, Holland.

Nutrition

THE INTERRELATIONSHIP BETWEEN BLOOD SUGAR, BLOOD CALCIUM, AND BLOOD COAGULABILITY. DONALD W. COWAN and HAROLD N. WRIGHT, Am. J. Physiol. **100:**40 (March) 1932.

The coagulation time of the blood in living animals may be decreased by injections of dextrose. Intravenous injections of dextrose are more effective in decreasing the coagulation time in jaundiced dogs than in normal dogs, not only in percentage of successes, but in the degree of shortening. Raising the blood sugar through injections of dextrose results in a heightened blood calcium as well as a heightened blood coagulability. The blood calcium more clearly parallels the blood coagulability curve than does the blood sugar curve after intravenous injection of dextrose. High carbohydrate forced feeding aids the coagulation time, decreasing the effect of intravenous injection of dextrose in jaundiced animals with damage to the liver.

NOURSE, Cleveland.

OTOLOGIC OBSERVATIONS IN CASES OF INTESTINAL INTOXICATION IN INFANTS. J. L. MAYBAUM, Arch. Otolaryng. **15:**418 (March) 1932.

Thirty-nine cases of intestinal intoxication in infants were studied in great detail from the otologic point of view. "The following otologic observations have been made as a result of these and other cases of intestinal intoxication in infants;

these conclusions having a direct bearing on the subject under discussion and tend to confirm our view that intestinal intoxication in infants is not of aural origin:

"Acute infection of the middle ear and mastoid is of frequent occurrence in infancy, and yet gastro-enteric symptoms are not commonly encountered in its course.

"Normal middle ears were present throughout in a majority of our cases of intestinal intoxication.

"A comparatively small number showed evidence of an acute otitis media that improved later, the symptoms of intoxication, however, remaining unchanged or becoming worse. Changes in the ear drums frequently occur in the agonal stages of many diseases.

"In a number of cases, the acute suppurative diseases of the middle ear apparently had no direct bearing on the presence of symptoms of intestinal intoxication, either antedating the onset of intestinal symptoms by one or more weeks or occurring independently late in the course of the intestinal complaint.

"Pathognomonic changes in the wall of the bony canal described by various writers were not observed in our cases.

"Accumulations in the middle ears or in the mastoid antrums of infants at autopsy are ante mortem in origin.

"Histopathologic examination of the middle ears and mastoids in a number of our cases failed to show any unusual observations." BARNETT, Chicago.

AVITAMINOSIS: III. PATHOLOGIC CHANGES IN TISSUES OF THE ALBINO RAT DURING EARLY STAGES OF VITAMIN A DEFICIENCY. H. S. THATCHER and BARNETT SURE, Arch. Path. **13**:756 (May) 1932.

In a study of fifty-three albino rats placed on a diet deficient in vitamin A, the following observations were made. During the early stages, that is, before a loss in weight occurred, metaplastic changes in the posterior part of the tongue, in the salivary glands and in the respiratory and urinary tracts were found. Some of the animals showed incipient ophthalmia or persistence of the cornified stage of the estrum. Bronchitis and pneumonia were also found in several animals. It is suggested that metaplasia of the epithelial structures in the respiratory tract of man may be the precursor of the common cold, bronchitis and bronchopneumonia, resulting from deficiency in vitamin A. LESLIE, Evanston, Ill.

MANGANESE, COPPER AND IRON CONTENT OF SERVING PORTIONS OF COMMON FOODS. M. A. HODGES and W. H. PETERSON, J. Am. Dietet. A. **7**:6 (June) 1931.

The authors note the increasing interest in the rôle of minerals in nutrition. Three of these minerals were investigated, and the amounts contained in serving portions of foods were estimated. Copper supplements iron in formation of hemoglobin. Manganese appears to improve the growth of animals and to stimulate blood regeneration in both secondary and pernicious anemia. The action of iron is recognized. The content of each in serving portions of 120 different foods is given. Manganese varies from 0.005 mg. in butter to 3.64 mg. in wheat bran; copper from 0.003 mg. in celery to 4.41 mg. in calf's liver and iron from 0.03 mg. in butter to 25 mg. in pork liver. The foods richest in manganese are wheat bran, blueberries, whole wheat, split peas, beets and navy beans. Those richest in copper are calf liver, oysters, beef liver, mushrooms, currants and chocolate. Those richest in iron are pork liver, spinach, lima beans, navy beans and chard.

The average daily intake of manganese, copper and iron for a child from 3 to 4 years of age is 0.8, 0.63 and 4.5 mg., respectively. Cereals supply the largest portion of manganese and copper. Vegetables and cereals furnish the most iron. Fruits are an important source of all three minerals.

An extensive bibliography is furnished. PARKER, Rochester, N. Y.

THE DETECTION OF INEFFICIENTLY PASTEURIZED MILK BASED ON A MODIFICATION OF THE NEW ROTHENFUSSER TEST. BERNARD S. GOULD, J. Dairy Sc. **15**:230 (May) 1932.

It is pointed out that the commercial pasteurization of milk is not always thorough and dependable. The tests used at the present time are not sufficiently accurate. The author has therefore proposed a new test; his experimental data seem to indicate that this test is reliable and practical. Pasteurization that is inadequate is thoroughly misleading and dangerous. Protection must be provided when it is expected, and the insurance which the label affords must have a basis.

CHAMPION, Cleveland,

THE EFFECTS OF LOW ENVIRONMENTAL TEMPERATURE UPON METABOLISM: I. TECHNIC AND RESPIRATORY QUOTIENT. RAYMOND W. SWIFT, J. Nutrition **5**:213 (May) 1932.

A detailed description of the technic and methods used in determining the basal metabolism of twenty-one men and women is given. Thirty-seven basal metabolism measurements were made, and one hundred and twelve observations were taken during exposure to the cold environment.

All procedure was rigidly checked and observed, so that it complied with the most recent and accepted information on the subject. Basal metabolism was first determined at room temperature (from 23 to 25 C.). The subject was then moved into the refrigerator for seventy-five minutes (temperature 2 C.; relative humidity, 80 per cent). No blanket, mattress or extra clothing was used. On the average, three ten minute samples of expired air, representing twenty, forty-five and seventy minute exposures to cold air, were collected. Efforts to avoid error due to *Auspumpung,* or blowing off of more carbon dioxide than is actually produced during the time of measurement, a result of hyperventilation, was believed to be successful.

The results, as deduced from the respiratory quotients obtained, indicate that exposure to cold does not favor preferential oxidation of carbohydrate. Therefore, depletion of the glycogen stores is merely associated with and in proportion to the increased total metabolism.

MUNNS, Winnetka, Ill.

THE EFFECTS OF LOW ENVIRONMENTAL TEMPERATURE UPON METABOLISM: II. THE INFLUENCE OF SHIVERING, SUBCUTANEOUS FAT AND SKIN TEMPERATURE ON HEAT PRODUCTION. RAYMOND W. SWIFT, J. Nutrition **5**: 227 (May) 1932.

Twenty-one persons were exposed in a basal condition for one hour and a quarter to an environmental temperature of 2 C. A complete description of the various experiments performed, together with an account of the technic used, is given. The results as summarized by the author were as follows:

1. There is no change in the protein metabolism corresponding to the increase in energy metabolism.

2. The blood sugar level remains unchanged, indicating that increased secretion of epinephrine is not involved.

3. There is no parallelism between the energy metabolism and pulse rate or respiratory rate, but distinct parallelism between heat production and respiratory volume.

4. The reaction to cold in a general way varies inversely as the amount of subcutaneous fat.

5. The increase in energy metabolism considered with the time spent in shivering shows that intense shivering increases the metabolism about 400 per cent.

6. The increase in metabolism shows no relationship to surface area.

7. The heat production is proportional to the amount and the intensity of shivering, and any increase in metabolism not accompanied by definite shivering may be justly ascribed to increased muscular tension.

8. The stimulus for shivering does not consist of even a slight drop in body (rectal) temperature.

9. Shivering begins when the skin attains a temperature of approximately 19 C.

MUNNS, Winnetka, Ill.

THE VALUE OF SOME VEGETABLES IN NUTRITIONAL ANEMIA. HAROLD LEVINE, F. B. CULP and C. B. ANDERSON, J. Nutrition **5**:295 (May) 1932.

Levine and his co-workers, Culp and Anderson, found, in reviewing the literature on nutritional anemia, that comparatively little work has been done with natural foods. Most investigators have used the ash of various foods in conducting their experiments, and, as the work of Bloom has indicated, the results obtained on the ash of vegetables cannot always be transferred to the natural foods.

The authors conducted experiments on rats in which the effects of dried spinach, lettuce, tomato, asparagus, broccoli and turnip greens on nutritional anemia were observed.

These carefully conducted experiments corroborate the work of other investigators and uncover several interesting and new considerations of the treatment of nutritional anemia. The results obtained in the feeding of the aforementioned dried vegetables demonstrate that such foods are of great importance in the maintenance of normal formation of blood.

The animals receiving the highest amounts of copper in their food experienced the most rapid blood regeneration. Combinations of vegetables, such as tomato (high copper content) and lettuce (high iron content), were found to be more effective than the use of either alone.

The vegetables were all fed at a level affording 0.2 mg. of iron but different amounts of copper. All combinations of the vegetables were effective in producing hemoglobin regeneration, and they are important sources of the minerals concerned in normal formation of blood.

MUNNS, Winnetka, Ill.

THE RELATIVE QUANTITIES OF THE HEAT-STABLE AND HEAT-LABILE FRACTIONS OF VITAMIN B IN RAW AND EVAPORATED MILK. LEO T. SAMUELS and FRED C. KOCH, J. Nutrition **5**:307 (May) 1932.

The authors consider the relative amounts of the vitamin B complex in fresh cow's milk and in evaporated milk important because of the increasing number of infants who are artificially fed and because evaporated milk is having widespread use as an infant food.

In their experiments, using rats as experimental animals, they set out to determine: (1) the separation of the two factors by fractionation of the milk solids and confirmation that the limiting factor is the heat-labile fraction. (2) the relative amounts of the heat-labile fraction in raw and in evaporated milks, and (3) the relative amounts of the heat-stable fraction in raw and in evaporated milks.

The growth experiments indicated that milk contains all the water-soluble vitamins necessary for the growth of the rat, but that relatively large volumes must be taken to obtain optimum growth. Commercial evaporation did not seriously affect these results.

Commercial evaporation probably destroys about from one-sixth to one-fifth of the antineuritic, heat-labile fraction. All cow's milk seemed to be quite low in this factor, however, and the authors believe it is wise to include other sources of these vitamins in the infant dietary. They found no identifiable destruction of the heat-stable, growth-promotion fraction during commercial evaporation. Milk is capable of adequately supplying this fraction for optimum growth. The amount necessary is fairly large but less than that required to supply an adequate antineuritic factor.

MUNNS, Winnetka, Ill.

THE EFFECT OF VITAMIN D IN INCREASING RESISTANCE TO INFECTION. E. C. ROBERTSON and J. R. Ross, J. Pediat. **1**:69 (July) 1932.

Four carefully controlled groups of rats were fed the same dose of Salmonella muriotitis (rat typhoid). Only 22 per cent of the rats previously fed a rachitogenic diet survived, as compared to 57 per cent of the rats fed the same diet with the addition of vitamin D. Of the rats exposed to fresh air and midday sun behind common window glass for two hours daily, 49 per cent of those on a rachitogenic diet survived the rat typhoid as opposed to 73 per cent of those on the same diet plus vitamin D.

The authors conclude that the addition of vitamin D in the form of vitamin D bread to a rachitogenic diet, which already contained considerable amounts of the other vitamins, raised the resistance of rats to a rat typhoid infection which was fed *per os*.

LEMASTER, Evanston, Ill.

DIETS IN PREGNANCY IN RELATION TO LOW BLOOD SERUM CALCIUM VALUES AT LACTATION. H. T. FRENCH and C. E. BOLSER, New England J. Med. **206**:14 (Jan. 7) 1932.

It has been shown that in high-bred cattle the condition known as milk fever, which accompanies the stage of mammary engorgement, and which in some instances is fatal, is accompanied by a marked fall in the level of the blood serum calcium, and may be checked either by pumping air into the mammary gland through the udder or by the intravenous injection of calcium salts.

Calcium determinations were made on a group of eighteen obstetric patients with the objective of determining the changes which take place in the level of this substance in the blood with the beginning of lactation.

The tendency of women with normal blood serum calcium at delivery is to show a fall of from 1 to 2 mg. (from 10 to 20 per cent) with engorgement of the breasts. This blood serum calcium then tends toward the original level, reaching this point within three or four days and remaining there.

In those who begin with low blood serum calciums, this stimulation comes at an earlier period, preceding lactation, and leads to an actual increase in the blood serum calcium at the time of beginning lactation instead of to the decrease noted in the first group; as in the first group, there is a continued stimulation which maintains the calcium level at the higher point.

Sixty per cent of the patients at parturition showed a calcium content well below the normal of from 10 to 12 mg. per hundred cubic centimeters. The larger number of these low values occurred during the late winter and early spring, while normal values tended to occur in the late summer, fall and early winter. This suggests a seasonal variation in these values.

In a pregnant woman, certainly from the sixth month on, there is a constant drain on calcium to supply the needs of the fetus in its bone development and other growth. It has been shown that even on well balanced diets it is difficult to maintain a positive calcium balance in either pregnant or lactating women, that with diets low in calcium there is a constant negative balance in normal women and that strongly acid diets tend to cause greater losses than neutral or slightly alkaline diets. If the food does not contain a sufficient supply, there is, of necessity, a drain on the mother's calcium depots, such as the trabeculae of the bones and teeth. Sherman states that most normal diets are too low in calcium, and that if this is true of normal diets, it must be increasingly true of diets of pregnant and lactating women with the increased demand of the fetus. The fetus, as well, may suffer from a lack of calcium in the mother's diet. Its bone formation may be affected, its teeth poorly formed and the tendency toward tetany and rickets increased.

Diets that contain a sufficient supply of calcium should help, and such a diet should contain sufficient fruit and vegetables to give a nearly neutral or slightly alkaline reaction to the residue, as diets consisting largely of meats, fats, sugars and starches result in an acid residue and lead to an increased elimination of

calcium, while diets with a slightly alkaline residue result in an increased retention of calcium. In addition to fruit and vegetables there should be in the diet between a pint and a quart of milk daily, meat once a day, one or two eggs daily and adequate bread and wheat cereal to supply the caloric needs. Calcium in the form of calcium lactate may be added to the amount of from 10 to 20 grains (0.6 to 1.3 Gm.) a day, with vitamin D in one of its several forms to aid in the absorption of calcium from the intestinal tract.

GENGENBACH, Denver.

ANOREXIA: A DAILY CLINICAL PROBLEM. WARREN QUILLIAN, South. M. J. **25**:759 (July) 1932.

The author concludes that anorexia is an important and widely prevalent clinical problem, that the psychic aspect constitutes the most frequent and difficult phase of this problem, and that education of the parents is an indispensable part of proper treatment. A complete physical survey in each instance is necessary to rule out a pathologic basis for the anorexia. Each case constitutes an individual problem and must be solved accordingly

SCHLUTZ, Chicago.

MOBILIZATION AND EXCRETION OF CALCIUM FOLLOWING OVERDOSAGE WITH IRRADIATED ERGOSTEROL. N. B. TAYLOR and C. B. WELD, Brit. J. Exper. Path. **13**:109, 1932.

The hypercalcemia following large doses of viosterol is due to withdrawal of calcium from the skeleton. Overdosage of viosterol depresses the power of the intestine to excrete calcium. The calcium mobilized from the bones accumulates in the serum. A certain level of serum calcium having been reached, an increase in the urinary calcium follows. Viosterol in the amounts that produce hypercalcemia does not increase absorption of calcium from the intestine.

AUTHORS' SUMMARY. [ARCH. PATH.]

EFFECT OF VITAMIN DEFICIENCY ON THE STRUCTURE OF THE THYROID AND THYMUS GLANDS. A. W. SPENCE, Brit. J. Exper. Path. **13**:157, 1932.

An attempt was made to produce lymphadenoid goiter in twenty-four young rats by means of a diet consisting of: white flour, 82 per cent; olive oil, 8 per cent; meat residue, 5 per cent; salt mixture (including an adequacy of potassium iodide), 5 per cent, and an unlimited supply of distilled water. The animals were on the diet for from nine weeks to thirteen months. Simple goiter was produced in fifteen of twenty rats examined, of which eight had slight goiters, five small goiters and two large goiters. Lymphadenoid goiter did not arise. The production of simple goiter was independent of an absolute iodine deficiency. The factors concerned were dietetic insufficiency and infection. Outstanding was the occurrence of keratinization cysts in the thyroid gland in twenty-three of the twenty-four animals. These cysts arose from the vesicles, probably as a result of exhaustion. Similar cysts were found in the thymus glands of three animals on the diet, and are considered to be large Hassall's corpuscles and not an effect of vitamin deficiency. No support was found for the hypothesis that the cysts in the thyroid and thymus glands represent distentions of the thyroid-thymic lymphatic glands.

AUTHOR'S SUMMARY. [ARCH. PATH.]

INFANTILE DIARRHOEA. A. V. NEALE, Brit. M. J. **2**:382 (Aug. 29) 1931.

The author discusses the incidence of infantile diarrhea in England and Wales and comments on its reduction in the past twenty-two or twenty-three years. He considers it largely a matter of the poorer population and stresses the importance of hygienic factors. There are certain uncontrollable factors, however, that cause fluctuation in the incidence, notably abnormally hot, dry seasons; he gives the summer of 1921 as an example. A brief comment is made as to the physiology of the alimentary tract and the relation between the narrow range of food that is

acceptable to the infant's digestion and the enzymes that are furnished by the intestines. Further comment is made as to the etiology, such as dysentery due to the bacilli of Sonne and Flexner, and various atypical forms of the paratyphoid bacilli. Occasionally strains of streptococci and pneumococci are recognizable. In a number of instances no demonstrable etiologic factor is present. The normal reaction of the intestinal content is stressed and various influences that diminish several of the enzymes. Trypsin, he states, is present from the earliest days of life and remains at a high level. He comments on the frequency with which parenteral influences are responsible for diarrhea. The effects of diarrhea are then discussed, particularly the rapid depletion of tissue fluids. Ketosis develops in many instances, and other disturbances in the acid-base equilibrium, producing in some instances acidemia and in others alkalemia, also develop. These changes result in a general disturbance of tissue functions, and the protective mechanism of the bowel is quickly removed. Secondary bacterial infections may occur after alteration in a physiologic function. The author thinks in some instances that the absorption of undigested protein through the damaged bowel may be responsible for some of the clinical features, such as intestinal intoxication and anaphylactic phenomena. The renal and hepatic functions are seriously disturbed by the dehydration and intoxication, and even degenerative changes may occur. Failure of the functions of these important organs may directly determine a fatal issue. The heart, especially the myocardium, is affected.

Acute ileocolitis has a characteristic sudden onset with diarrhea, with or without vomiting. The stools are frequent, mucus and blood being visible usually. Abdominal pain and tenesmus may occur; Flexner or Sonne bacilli may or may not be demonstrated as well as others. These processes not only result in a toxemia but also in damage amounting in some instances to necrosis of the mucosa.

Fermentative diarrhea is associated with acidic, gaseous, frothy, highly irritating, offensive stools which cause excoriation of the skin. Dehydration is sometimes extreme. Fever may be minimal or absent, or even subnormal. The infant is essentially suffering from starvation, dehydration and much physical discomfort. The fermentation arises from irregular feeding or overfeeding of carbohydrates and fats, which may be directly due to temporary depletion of the normal digestive enzymes, similar to that occurring in parenteral infection. Infections of the mouth sometimes occur.

Acute alimentary intoxication is a serious disorder, which may arise from the ingestion of bacterial or chemical toxic material, as from the absorption of decomposition products from intestinal fermentation. It may aggravate the course of a simple fermentative diarrhea. Stools are watery, and vomiting occurs; the more typical clinical picture is marked collapse, subnormal temperature, rapid feeble pulse, scanty urine, clammy skin, pallor and sighing respiration. Convulsive movements may occur. Sometimes the suggestion is that of an anaphylactic shock. Dehydration also is a serious complication. A diagnosis is made by taking a careful and accurate history of the disorder; a consideration of the quality of food eaten and a careful examination of the stools are necessary for indications of toxemia. The degree of anemia, which may be rapid or slow, may also indicate toxemia. Depression of the fontanel; dry, inelastic skin, sunken eyes, rapid loss in weight and small urinary secretion denote at a glance the degree of dehydration. Meningismus is not uncommon, and acute intussusception, the author states, may arise, due to irregular intestinal movements.

In treatment the nursing is important, and fluids are still more important. The author states that all milk should be stopped for twenty-four hours and replaced by pure water, a quarter-strength physiologic solution of weak tea, Ringer's solution and sometimes dextrose. Gentle rectal lavage with warm saline solution has proved beneficial. Sterile fluids should be given by parenteral routes, and the renal and hepatic functions should be aided in the detoxicating and eliminative processes.

Water should be administered by subcutaneous injections, and a solution of dextrose by injection into the superior longitudinal sinus or into the internal saphenous vein, or an intraperitoneal injection of saline solution or dextrose may

be used. Blood transfusions are valuable later, 15 cc. per pound of body weight being the usual guide. The blood transfusion tends to compensate for the loss of protein. All parenteral infections must be removed. The author states that antidysentery serum, given intramuscularly, is efficacious in some cases of acute dysenteric ileocolitis.

Drugs form a small part in the management of infantile diarrhea. Morphine is dangerous; atrophine is sometimes used to check spasm and pain. The best food is breast milk; next, easily assimilable forms of carbohydrates and buttermilk. The author stresses that the biochemistry of the body tissues must be kept constantly in mind.

ROYSTER, University, Va.

THE USE OF VITAMIN B IN CASES OF OEDEMA. D. W. CARMALT-JONES, Brit. M. J. **1**:374 (Feb. 27) 1932.

Following the use of vitamin B in what is described as the "beriberi heart" for the purpose of reducing edema, the author decided to try it in other cases. After citing three cases of failure either to save life or markedly to reduce the edema and explaining the reasons for these failures, he then cites several other cases in which satisfactory reduction of edema followed the administration of vitamin B. The first case was one of secondary anemia in a middle-aged woman with marked edema. Both diuresis and discharge of fluid from the bowel took place, and the edema subsided rapidly. The second was a case of hemiplegia with edema. The third and fourth were cases of pernicious anemia with edema. All of the patients were adults. The preparation used was tikitiki, which contains only vitamin B_1 and is made by the government of the Philippine Islands. The other preparation used was marmite which was not found as efficient as tikitiki.

ROYSTER, University, Va.

THE EFFECT OF PARBOILING AND MILLING ON THE ANTINEURITIC (B_1) AND PHOSPHATE CONTENT OF RICE. W. R. AYKROYD, J. Hyg. **32**:184 (April) 1932.

This work includes experimentation on animals and determinations of phosphorus. Rice that has been parboiled in its preparation as an aid in removing the husk retains much more vitamin B value than does rice that has not been parboiled in removing the outer layers. This is because the steamed rice absorbs water and, along with it, the water-soluble vitamins, as well as phosphate from the outer layers. The phosphate content of the prepared product is a fair index of the amount of vitamin B_1 contained.

JANNEY, Milwaukee.

THE TOXICITY OF IRRADIATED ERGOSTEROL. J. B. DUGUID, M. M. DUGGAN and J. GOUGH, J. Path. & Bact. **35**:209, 1932.

Viosterol was found to be more toxic in rats fed on a certain synthetic vitamin-free diet of high calcium content than in rats on a normal diet. The absence of vitamins and the high calcium content were considered as possible determinants of the toxicity, and the high calcium content was found to be the more powerful. After reduction of the calcium and also of the phosphorus content of the diet, the evidence suggested that the absence of vitamins also contributed to the condition, but the evidence of this is not accepted as convincing. The toxicity was estimated chiefly on arterial and renal calcification. The reliability of these lesions as criteria is discussed. Arterial lesions are accepted as reliable indications of viosterol poisoning in the rat. Renal lesions in viosterol poisoning were noted to occur in two forms, namely, calcification of the renal arterioles, and calcareous casts in the renal tubules. The former appeared as part of a general arterial involvement and, as such, was taken as a reliable indication. The latter was found to be a lesion of too common occurrence in the rat, independently of the administration of viosterol, to be admitted as reliable evidence of toxicity.

AUTHORS' SUMMARY. [ARCH. PATH.]

PRACTICAL POINTS ON MODERN INFANT FEEDING. BERNARD MYERS, Practitioner **128**:425 (April) 1932.

The author, after an experience of over twenty-five years in feeding several thousand babies, offers many practical suggestions regarding the feeding of infants. He stresses the need of watching for symptoms of infection whenever digestive processes suffer, and tolerance for food is lowered.

Due consideration is given to basic requirements of infants. Myers devotes special attention to the use of acid milk. He discusses this subject in detail and gives several examples of patients fed on acid milk.

SAPPINGTON, San Francisco.

Prenatal Conditions

CONGENITAL CYST OF THE LUNG. HAROLD L. STEWART, PATRICK J. KENNEDY and ALFRED E. JAMES, Arch. Path. **14**:627 (Nov.) 1932.

A case of congenital cyst of the lung in a woman, aged 54, is reported. The majority of the distended bronchi communicated with the main bronchial tree, but a few had no such connection and were therefore true cysts. Hypertrophy of the right side of the heart, sclerosis of the pulmonary artery and polycythemia were also found. On physical examination a sound indistinguishable from a pleural friction rub was heard, but there was no pleuritis to cause it. Roentgenograms of the chest during life simulated chronic pulmonary tuberculosis with cavitation.

LEMASTER, Evanston, Ill.

TRUNCUS ARTERIOSUS COMMUNIS PERSISTENS: CRITERIA FOR IDENTIFICATION OF THE COMMON ARTERIAL TRUNK WITH REPORT OF A CASE WITH FOUR SEMILUNAR CUSPS. ELEANOR M. HUMPHREYS, Arch. Path. **14**:671 (Nov.) 1932.

The theories of the manner of development of the septums of the trunk and cardiac bulb are reviewed, as well as those pertaining to some of the defects commonly associated with imperfect development of these septums. A case of truncus arteriosus communis with four semilunar cusps is reported. The most widely accepted cases of persistent common trunk are reviewed and analyzed. Criteria for identification of the common arterial trunk are discussed.

LEMASTER, Evanston, Ill.

INTRAUTERINE PNEUMONIA WITH EVIDENCE OF HEALING: REPORT OF A CASE. EDWARD DYER ANDERSON and JOHN F. POHL, J. Pediat. **1**:608 (Nov.) 1932.

Cases of fetal pneumonia reported in the literature have shown microscopic changes in the lungs regarded as representing a very early pneumonia or the response to an overwhelming infection. The case described by Anderson and Pohl was that of a full-term, new-born infant who died on the fourth day of life, and is the first instance reported in which the lungs showed organization of an inflammatory exudate and fibrosis of the pulmonary tissue which would indicate that the fetal lung might react defensively toward an infection in the same manner as is possible after birth.

LEMASTER, Evanston, Ill.

CONGENITAL HEART DISEASE. GEORGE KARL FENN and CARL A. JOHNSON, M. Clin. North America **16**:293 (Sept.) 1932.

Cases of congenital heart disease may be divided into two large groups, the cyanotic and the noncyanotic. The causes of the cyanosis are not yet perfectly understood, but the principal factor seems to be the mixture of venous with arterial blood. Contributing factors are insufficient oxygenation in the lungs and increased consumption of oxygen in the tissues owing to capillary stasis. That cyanosis is not due entirely to lack of oxygenation is indicated by the fact that

inhalations of oxygen will not remove it. Also observations at autopsy show that consistent pulmonary stenosis without septal defect will not produce the same degree of cyanosis as occurs when a venous-arterial shunt through a septal defect is present. Several cases are described illustrating the common types of congenital heart disease, viz., septal defects, stenosis of the orifices and persistence of fetal pathways.

SMITH, Ogden, Utah.

PREMATURE INFANTS. JULIUS H. HESS, M. Clin. North America **16**:477 (Sept.) 1932.

The smallest infant that Hess has been able to rear successfully weighed 745 Gm. Of 1,112 infants admitted to the station for premature infants with which he is connected, 805 lived and were transferred to their homes. He is convinced that breast feeding lowers morbidity and mortality to a very large degree. It is advisable, however, not to feed an infant milk of an eclamptic mother before the eighth day, and to do so after that time only if she is free from symptoms. An infant requires about one sixth of its body weight of water (inclusive of that in milk) in twenty-four hours. This amount should be reached at about the fourth day. Feedings are begun with small amounts, from 2 to 6 cc., and gradually increased. To fulfil all the infant's needs, from 140 to 160 cc. of breast milk per kilogram will be required. This amount should be reached after the first month. Skimmed lactic milk or powdered skimmed lactic milk may be added to mother's milk. Orange juice should be added by the third week and cod liver oil at about the same time. Raw egg may be gradually added to the milk. The infant should be given short exposures to violet rays three times a week.

Most premature infants with cerebral injuries are inclined to be somnolent. Of 246 who died at the station and came to autopsy, 43 per cent had intracranial hemorrhage. Of 64 infants who survived this condition, 44 are normal, one has hydrocephalus, 8 show disturbance of reflexes with spasticity, 7 have moderate increase of reflexes without spasticity, and 4 are mentally retarded. It is not always possible to differentiate congestion and hemorrhage by the character of the spinal fluid. In 35 proved cases of hemorrhage and acute cerebral congestion, the fluid was grossly bloody or hazy in 80 per cent. In 42 cases without evidence of hemorrhage at necropsy, the fluid was bloody or hazy in 31 per cent.

A diagnosis of syphilis was made in only 5.5 per cent of 1,041 patients admitted. The mortality in these cases was almost 50 per cent. The treatment preferred is mercury, either in the form of mercury with chalk or as inunctions. Stovarsol is also of service, either alone or with mercurials.

SMITH, Ogden, Utah.

FOETAL ASCITES. RICHARD H. HUNTER, Lancet **2**:999 (Nov. 5) 1932.

Fetal ascites has been ascribed to many causes, among them: (*a*) obstruction to the portal circulation, due to perihepatitis, syphilitic gumma or tumors pressing on the portal vein; (*b*) chronic peritonitis due to syphilis; (*c*) tumors or a distended bladder pressing on the large vessels of the abdomen; (*d*) hypoplasia of the urinary organs, and (*e*) defects in the circulatory systems.

Four cases are described. The first, though described as one of "fetal ascites," was really a case of arrested development of the hind end of the fetus. It showed an enormously distended urogenital sinus and ventral cloaca. The second case also showed great abdominal distention. Three pints of fluid escaped when the abodmen was opened. The liver was small and nodular. The diagnosis of atrophic multilobular cirrhosis was confirmed by microscopic examination, the apparent cause being fetal syphilis. In the third case the general appearance was that of generalized edema. The spleen was enormously enlarged. The portal and splenic veins were small and their lumen was extremely small. In the fourth case also there was generalized edema, an early stage of polycystic disease of the kidneys was noted.

LANGMANN, New York.

CONGENITAL DEFECT OF THE TIBIA. C. ALETTER, Frankfurt. Ztschr. f. Path. **43**:196, 1932.

The right tibia was missing. The left proximal portion of the left tibia was normal, but its distal portion was abnormally developed. Both patellae were absent. There also were malformations in both ankle joints.

SAPHIR, Chicago. [ARCH. PATH.]

PROSOPOTHORACOPAGUS. O. WALBAUM, Virchows Arch. f. path. Anat. **280**:275, 1931.

The monstrosity described is compared with previously reported similar ones and with six thoracopagi studied by the author. The main feature that distinguishes double monsters with fusion of both face and thorax from those with fusion of the thorax alone is the single pharynx, esophagus and stomach of the former.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

CONGENITAL DIVERTICULUM OF THE CECUM. B. ODQVIST and T. PETREN, Virchows Arch. f. path. Anat. **280**:581, 1931.

After a brief discussion of some of the more unusual forms of congenital diverticulum of the intestine, the authors present a description of a diverticulum of the cecum that was observed by chance during necropsy on a girl, aged 3 years. A typical Meckel's diverticulum was situated 90 cm. above the ileocecal valve. The appendix was given off from the cecum in the normal position. Arising in the angle formed by the junction of the ileum with the large bowel was a blind diverticulum 6 cm. long by 2.5 to 3 cm. in diameter. It possessed a mesentery in common with the appendix. Its lumen communicated with that of the intestine. Its wall was composed of a mucosa, submucosa, inner muscular coat and external muscular coat. The authors do not consider the structure a reduplicated appendix or a bifurcated cecum, but a congenital diverticulum of the cecum.

SCHULTZ, Chicago. [ARCH. PATH.]

DEVELOPMENT ANOMALIES ASSOCIATED WITH ABSENCE OF THE CAUDAL END OF THE VERTEBRAL COLUMN. A. FELLER and H. STERNBERG, Virchows Arch. f. path. Anat. **280**:649, 1931.

The authors give a detailed account of the conditions found in two monstrosities of the sympus apus type and compare them with the conditions found in two other monstrosities with maldevelopment of the lower extremities. Maldevelopments associated with defects of the lower end of the vertebral canal they classify as monopus, sirenoid monopus and siren. The term monopus they would reserve for the anomaly in which the vertebral defect is asymmetrical and involves one side only, leading to the failure of development of one posterior limb. Sirenoid monopus they would apply to the monstrosity in which the asymmetrical defect involves also the midportion of the lower vertebral column. Siren is applied to the anomaly associated with a median and bilaterally symmetrical vertebral defect. The absence of the allantois and of one umbilical artery in siren indicates the very early stage of embryonic development during which the maldevelopment arises. The latter is not due to fusion of two limbs or regression of one limb bud or to external factors, but is due to factors inherent in the germ plasm which result in the lack of formation of sufficient tissue for two limb buds.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

Acute Infections

EPIDEMIOLOGY OF DIPHTHERIA. EDWARD S. GODFREY, JR., Am. J. Pub. Health **22**:237 (March) 1932.

Immunization of children from 5 to 14 years of age has only a fraction of the value in stemming epidemics of diphtheria that immunization of children

below 5 years has. If 30 per cent of the latter group is immunized, the diphtheria rate can be favorably controlled.

Graphs of many cities show that the incidence of diphtheria was little affected by immunization of 50 per cent or more of the group from 5 to 9 years of age, but that it declined sharply on immunization of 30 per cent or more of the group aged 4 years and less.

It is suggested that more attention should be directed to this younger group, since the results of immunization of children of these ages are much more promising.

The question of carriers is considered. The author feels that carriers tend to develop carriers (and, presumably, immunity), while cases tend to develop new cases.

PARKER, Rochester, N. Y.

BRUCELLA ABORTUS INFECTION IN INFANCY AND CHILDHOOD. JOHN P. HUBBARD, J. Pediat. **1**:464 (Oct.) 1932.

A review of the literature on Brucella abortus infection indicates the infrequency of the disease in the younger age groups. A case of Brucella abortus infection in a 6 year old boy is presented, in which the history and clinical course were typical and in which the agglutination reaction, blood culture and urine culture were positive. Among 111 patients in whom Brucella abortus infection was considered, the patient whose case is reported was the only one presenting a positive agglutination reaction.

LEMASTER, Evanston, Ill.

AN EVALUATION OF DIPHTHERIA IMMUNIZATION. H. E. THELANDER and K. KILGARIFF, J. Pediat. **1**:470 (Oct.) 1932.

Many problems relating to diphtheria immunization are discussed, and the literature on this subject is quoted extensively. The authors compare the results of injections of both toxoid and toxin-antitoxin, given at varying intervals and in different doses. This study covers the practical aspect of this subject thoroughly.

LEMASTER, Evanston, Ill.

BRUCELLA ABORTUS IN MILK. J. SMITH, J. Hyg. **32**:354 (July) 1932.

Frequent cases of undulant fever in man of obscure origin have caused study, which suggests that infections occur through the ingestion of milk containing Brucella abortus. Authors have found samples of milk infected in a frequency varying from 5.7 to 30 per cent. A study of the thermal death-point of Br. abortus is presented.

In samples of raw milk from 279 different sources, 28.3 per cent were found to contain Br. abortus by the inoculation of guinea-pigs with a suspension containing this organism, and 10.3 per cent were found to contain tubercle bacilli. Among 187 samples obtained from 3 different plants, in which the milk was pasteurized by the "holding" method, no Br. abortus was found, and 2.1 per cent of the samples showed only tubercle bacilli. After the "flash-point" pasteurization method, 18.7 per cent of 192 samples contained Br. abortus and 9.8 per cent tubercle bacilli. This indicates that the flash method of pasteurization as performed on these samples of milk was quite inadequate.

JANNEY, Milwaukee.

RABIES. P. REMLINGER and J. BAILEY, Ann. Inst. Pasteur **47**:608, 1931.

The article, apparently the first of a series, presents various phases of the activity of the virus. The virus was often demonstrated in the spleens of various infected animals, most frequently in those of cats (seven of fifteen animals). The liver and kidneys also yielded the virus. Certain areas in the nervous system were occasionally encountered in which there was no virus. A study of five fixed viruses confirmed the idea that these vary in virulence and in symptoms produced. Frogs

and toads were found to be completely refractory. "The passage of fixed virus into the central nervous system of vaccinated animals is no more a question of strain than of the method of treatment or of the animal used." Dilution was found not to attenuate the virus. A review of four cases in which repeated vaccination was practiced (in one, four times in four years) indicated that no untoward reactions should be expected.

M. S. MARSHALL. [ARCH. PATH.]

HISTOLOGIC CHANGES OF THE BONE MARROW AND THE FINDING OF MICRO-ORGANISMS IN LEISHMANIASIS OF CHILDREN. F. RUBINI, Riv. di clin. pediat. **30**:773 (June) 1932.

In seven children with leishmaniasis, bone marrow punctures and smears were made. The puncture was done at the epiphysis of the tibia.

In the cases in which the number of organisms seen in the bone marrow smears were few, there was found marked proliferation of the erythropoietic elements of the bone marrow, similar to that found normally in the first three days of life or in the premature infant. Where the number of organisms, however, was large, there was no difference between the erythropoietic cells and those of normal children.

HIGGINS, Boston.

RARE COMPLICATIONS OF SCARLET FEVER. B. S. HIRSCHBERG, Jahrb. f. Kinderh. **136**:243 (Aug.) 1932.

In a case of mild scarlet fever, on the sixth day, streptococcic peritonitis developed and on the seventh day death occurred. Autopsy revealed no other complications.

In a case of moderately severe scarlet fever, complicated by bilateral otitis media and later by purulent ethmoiditis, both complicating conditions apparently subsided. On the fifty-fourth day, headache and vomiting occurred, and on the fifty-sixth day coma. The neck was stiff; Kernig's and Trousseau's signs were positive, and the pupils were sluggish. Death occurred. Autopsy revealed meningitis over the base of the frontal lobes and over portions of the cerebellum, an abscess under the corpus caudatum and pus in the lateral ventricle. Streptococci were present.

In case 3, death occurred on the thirtieth day, following signs of meningitis. Autopsy showed acute nephritis and several cerebral abscesses.

In case 4 (observed by Dr. Awdejeff) the onset of scarlet fever was severe. There were bilateral otitis media and long-continued fever. Death occurred suddenly on the fiftieth day. Section revealed rupture of the aorta 6 cm. beyond the valves, due to abscess in the wall of the vessel.

CLAUSEN, Rochester, N. Y.

HEPATITIS AND CHOLECYSTITIS: A SPECIFIC TOXIC COMPLICATION OF SCARLET FEVER. H. SCHOTTMÜLLER, Klin. Wchnschr. **10**:17 (Jan. 3) 1931.

The author reports five cases in children from 3 to 12 years old. The onset of the complication was in the second, third or fourth week with fever, pain in the upper part of the abdomen and swelling of the liver. Although disease of the gallbladder is extremely rare in children ordinarily, in this instance only children were affected. The abdominal pain comes on suddenly and is poorly localized, although older children may point to the upper part of the abdomen. Occasionally pain may be absent, but routine examination reveals enlargement of the liver. The enlargement of the liver varies from 1 to 3 finger breadths, and the gallbladder is also enlarged in some cases. The liver returns to its normal size in about one or two weeks. One case showed icterus. Schottmüller believes that the condition is due not to swelling of the portal lymph nodes but to toxic damage of the walls of the biliary ducts. In addition to the evidence of enlargement on the liver and gallbladder, there were fever and leukocytosis with eosino-

philia. To be sure, the latter symptoms may also be due to other complications of scarlet fever, and in some cases there was present at the time adenitis or scarlet fever rheumatism. The fact that as a rule the prognosis is favorable may be the reason that from the histopathologic standpoint this complication is less known than from clinical experience. The author notes the following statistics: In the last twenty years, from 1910 to 1929, 5,945 patients with scarlet fever were admitted to the clinic; in only eight of the one hundred and fifty-two autopsies was there evidence of enlargement and inflammation of the gallbladder and liver. As to the pathogenesis of this condition, Schottmüller believes that the benignity of the process speaks against the invasion of the liver by hemolytic streptococci. He maintains that the hemolytic streptococcus is the etiologic agent of scarlet fever, despite the objections of Cantacuzène. He has seen this complication only in scarlet fever, never in any other streptococcus disease, and, therefore, considers it to be specific to scarlet fever. He believes that two other complications might result from the same toxic material, namely, scarlet fever rheumatoid disease and scarlet fever nephritis. Whether the slight icterus which goes with the exanthem of scarlet fever might be in some way related to the complication herein described cannot be answered at present, although it has been shown that in the first days of scarlet fever there is usually found an increase in the bilirubin content of the blood.

SILVERMAN, Syracuse, N. Y.

PROLIFERATIVE HEPATITIS AND CHOLECYSTITIS IN SCARLET FEVER. T. FAHR, Klin. Wchnschr. **10**:17 (Jan. 3) 1931.

Fahr describes the result of the autopsy in one of the cases reported by Schottmüller (Klin. Wchnschr. **10**:62 [Jan. 10] 1931). The patient was a 6 year old boy in whom scarlet fever was complicated by inflammation of the liver and gallbladder. Death was caused by peritonitis due to an infarct of the spleen. The most noteworthy changes were proliferations in the kidneys and especially in the liver and gallbladder. In the liver the proliferation seemed to be most pronounced about the smaller bile ducts and about the veins. In the gallbladder the mucosa was thickened and there were diffuse infiltrations in the wall similar to those in the kidneys. These changes, Fahr believes, have a hematogenous toxic origin. The histologic appearance is absolutely against bacterial invasion. He believes that the condition is an allergic phenomenon in the course of the streptococcic infection, and that the reaction that is necessary for the development of the changes is produced particularly in scarlet fever.

SILVERMAN, Syracuse, N. Y.

CAUSES OF MALIGNANT COURSE OF DIPHTHERIA. J. KOSCHATE, Klin. Wchnschr. **10**:62 (Jan. 10) 1931.

Serum from cases of diphtheria was used in the preparation of culture mediums for the growing of a known virulent strain, and the toxin was tested in guinea-pigs. Of twenty animals tested only those two died which were inoculated with the toxin of the organism grown on culture mediums containing serum from children with malignant diphtheria. A given strain of the diphtheria bacillus grown on serum from a malignant case produced even in the first generation smaller forms with fewer polar bodies than when grown on serum of normal children.

SILVERMAN, Syracuse, N. Y.

TREATMENT OF ERYSIPELAS WITH ROENTGEN RAYS. E. NOTGER VON OETTINGEN, München. med. Wchnschr. **79**:1640 (Oct. 7) 1932.

Von Oettingen tabulates the results in about 225 cases of erysipelas in which the patients were treated with roentgenotherapy at various clinics. A critical drop in temperature occurred in from 40 to 70 per cent of the cases in various series. A fall in temperature by lysis occurred in from 10 to 25 per cent of

the cases. Recurrences or poor results were infrequent. Von Oettingen reports his own seventy-eight cases in which the patients were hospitalized; thirty-seven patients had a critical drop in temperature, twenty-five had a gradual decline of the temperature, and in sixteen the treatment was not successful.

The dosage used was from 10 to 25 per cent of an erythema dose. Only the infected areas were exposed to the roentgen rays. The treatment was repeated in forty-eight hours if there was evidence of the spreading of the infection or if the general symptoms did not improve. No more than three exposures were given. The treatments were well tolerated.

No mention is made of the ages of the patients or the location of the lesions, both of which are important in the evaluation of any type of therapy. The author condemns the treatment by local applications but makes no mention of serotherapy or exposure to ultraviolet light. BRAHDY, Mount Vernon, N. Y.

HISTOLOGIC PICTURE OF RHEUMATIC FEVER: V. OCCURRENCE OF STREPTOCOCCI IN THE EARLY LESIONS (FRÜHINFILTRAT) OF RHEUMATIC FEVER. F. KLINGE and C. MCEWEN, Virchows Arch. f. path. Anat. **283**:425, 1932.

In previous papers, Klinge has described the early histologic lesions of rheumatic fever that are present prior to the development of Aschoff bodies. The organs of two patients, whose death occurred about three weeks after the beginning of acute rheumatic disease, were examined for bacteria. In addition, cutaneous nodules of patients suffering from rheumatic disease were obtained for biopsy. Serial sections were made, which were stained according to Gram's method; every tenth section was stained with hematoxylin-eosin. The authors came to the conclusion that generally no bacteria could be found histologically. Wherever they were present, their position and pleomorphism prohibited consideration of them as the cause of the lesions. These negative results do not necessarily indicate that streptococci are not the cause of rheumatic fever if one considers it as an allergic disease. The authors could show that if 200,000 nonhemolytic streptococci were injected into normal rabbits a cutaneous lesion was produced of the same size as that seen in a sensitized animal after the injection of twenty bacteria. These lesions were excised after forty-eight hours and stained in series by the Gram method. In the normal animals partially degenerated streptococci were occasionally found in the tissues. In the sensitized animals, not one streptococcus was found. SCHOENTHAL, New York.

PATHOLOGICO-ANATOMIC CHANGES NOTED IN THE MIXED EPIDEMIC OF SCARLET FEVER AND DIPHTHERIA IN TALLINN (DORPAT)-REVAL (ESTHLAND) FROM 1926 TO 1927. R. STANKIEVITZ, Virchows Arch. f. path. Anat. **284**: 1, 1932.

This epidemic has been described from the clinical point of view by von Bormann (*Ztschr. f. Kinderh.* **46**:233, 1928). From Oct. 1, 1926, to June 1, 1927, one hundred and sixty-two patients were admitted to the hospital with the diagnosis of scarlatina and diphtheria, sixty-four (40 per cent) of whom died. The greatest mortality was observed during the first ten years of life. In nearly all cases hemolytic streptococci and diphtheria bacilli were recovered from the throat ante and post mortem.

This paper deals with pathologico-anatomic changes of the kidneys of thirty patients. According to Fahr's classification, the cases were divided into three groups: nephrosis, nephritis and mixed forms. Eleven cases of nephrosis were observed; seven of these showed a relatively pure picture of tubular degeneration with very slight changes of the glomeruli (nephrosis tubularis II, Fahr); in four other cases the changes in the glomeruli were more marked, and they were considered as "glomerulonephrosis." Ten cases of glomerulonephritis were seen. They were divided into two groups, the early and late. In six cases in which death occurred from two to three weeks after the onset of the disease the

ordinary changes of glomerulonephritis with varying involvement of the tubules were found; in four patients who died during the early days of the disease marked glomerulitis was present. The third group (nine cases) showed interstitial changes in the cortex of the kidneys (plasmolymphatic infiltrations) in addition to the more or less marked changes of the glomeruli and tubules. This form was classified as nephritis lymphatica acuta et glomerulonephritis acuta.

The author discussed the pathogenesis of these different types of Bright's disease. He attributes the glomerulonephrosis to the combined effect of streptococci and diphtheria bacilli, since it does not occur in pure diphtheria. According to his opinion, nephritis acuta lymphatica is an early form of the scarlatina nephritis, which is produced by the ectotoxin of Streptococcus scarlatinae; glomerulonephritis acuta is caused by its endotoxin. The development of the different types of Bright's disease seems to depend on the stage of immunity of the organism, the time of invasion, the virulence of the bacteria and the combined effect of their toxins.

SCHOENTHAL, New York.

ACTIVE IMMUNIZATION AGAINST DIPHTHERIA. M. P. ISABOLINSKI, B. P. KARPATSCHEWSKAJA and W. F. TOWJANSKAJA, Ztschr. f. Immunitätsforsch. u. exper. Therap. **73**:27, 1931.

Active immunization with Ramon's anatoxin lowered the morbidity from seven to ten times in 4,185 children. The local and general reactions were of no significance. The percutaneous method of Loewenstein is strongly recommended.

I. DAVIDSOHN. [ARCH. PATH.]

LOCAL LEUKOCYTIC REACTION AFTER VACCINATION. HEINZ N. BRINNITZER, Ztschr. f. Kinderh. **53**:133, 1932.

In a previous study the author found no characteristic leukocytic reaction after vaccination, except a "shift to the left" in most instances and an increase in plasma cells in about 50 per cent of the cases (twenty). This, however, is only a reaction to inflammation and is not specific for vaccination. In the present study the local leukocytic reaction was studied daily for a period of from fourteen to sixteen days after vaccination. Control blood was drawn from a similar area on the side not vaccinated and also from unvaccinated children given injections of human lymph. No characteristic blood picture was found, and again the "shift to the left" and increase in plasma and lymph cells were noted.

SHELLING, Baltimore.

TREATMENT OF PERTUSSIS WITH INTRAMUSCULAR INJECTIONS OF BLOOD. S. CSAGOLY, Orvosi hetil. **76**:55 (Jan. 23) 1932.

In a series of seventy-one patients, the author systematically injected convalescent serum or adult blood. Convalescent serum was available in only three cases, and in these improvement was seen within six days. For the other cases, the blood of a member of the family was used, and in these the improvement was also satisfactory, as most of the patients stopped coughing within from eight to ten days. The author emphasizes that convalescent serum is preferable to adult blood, and also advises that the injections be given as early as possible.

ZENTAY, St. Louis.

ACTIVE IMMUNIZATION AGAINST CHICKENPOX. Z. GULÁCSY, Orvosi hetil. **76**: 296 (April 9) 1932.

In connection with an annoying epidemic of varicella in the Children's Hospital, the author began active immunization of all children who at that time were in the hospital. Thirty-eight children were immunized. With the exception of five children on whom scarification was done, all were vaccinated with the intracutaneous method. The vaccine was taken from a fresh vesicle and diluted with

physiologic solution of sodium chloride (1:10). Of this dilution 0.1 cc. was injected intracutaneously. In all cases of intracutaneous vaccination the vesicle appeared on about the thirteenth day. In three of the children who were immunized by scarification no reaction developed. The results are satisfactory, and it seems that the immunization is independent of the local reaction. The vaccination produced the same blood picture as chickenpox itself.

ZENTAY, St. Louis.

ACTIVE MEDICINAL TREATMENT OF GRIPPAL INFECTIONS IN INFANTS AND YOUNG CHILDREN. G. PETRÁNYI, Orvosi hetil. **76**:298 (April 9) 1932.

The author gave much higher doses of amidopyrine than usual for the treatment of grippal infections in infants and children. The dosage according to age was as follows: up to 1 month, 0.05 Gm.; from 3 to 6 months, 0.10 Gm.; from 6 to 12 months, 0.15 Gm.; from 2 to 4 years, 0.20 Gm., and over 4 years, from 0.20 to 0.25 Gm. every two hours during the day and night. The author reports that the temperature drops promptly and without any unpleasant symptoms. He thinks that with such dosage amidopyrine is a useful drug in the treatment of grip. No toxic effects have been noted even after protracted use. Infants and children with pneumonia treated with amidopyrine seem to stand the infection better and regain appetite promptly, and fever and general symptoms disappear more promptly. If amidopyrine does not reduce the temperature or if, after an initial decrease, it rises again, as a rule a fatal complication must be considered.

ZENTAY, St. Louis.

Internal Diseases

THE TREATMENT OF COUGHS WITH SUPRARENAL: I. RESPIRATORY INFECTIONS. ORVILLE BARBOUR, Arch. Pediat. **49**:681 (Oct.) 1932.

The author summarizes his article thus:

"During the past 18 months I have administered suprarenal, and, in refractory cases, thyroid, to 178 cases of upper respiratory infection, in which the predominant symptom was coughing.

"A careful consideration of the scientific principles involved, a review of the experimental and clinical observations of others, and a deliberate study of my clinical results have convinced me of the soundness and efficacy of the endocrine therapy.

"The results of this investigation, in my opinion, indicate that one may expect suprarenal, and at times thyroid, in appropriate doses, to be successful in relieving 90 per cent, or more of cases of upper respiratory coughs in infants and children.

"The suprarenal, and, in refractory cases, thyroid, appear not only to promptly relieve the coughing, but also seem definitely helpful toward improving the condition and health in general of the patients.

"Realizing my limitations in pathologic and experimental facilities and knowledge, I am herein submitting my observations to those who have the facilities and knowledge to prove or disprove my observations and interpretations."

AUTHOR'S SUMMARY.

AN OSTEOBLASTIC OSTEOID TISSUE-FORMING TUMOR OF A METACARPAL BONE. HENRY L. JAFFE and LEO MAYER, Arch. Surg. **24**:550 (April) 1932.

A tumor of the fourth metacarpal bone was described. It began when the patient, a girl, was 12 years of age. After growing slowly for almost three years, it began to grow rapidly. The tumor mass was removed; it measured 10 by 6.5 by 6 cm. Only the articular head of the metacarpal bone remained. The tumor was of such consistency that it could be cut with a knife, but it was granular and firm. Histologically, it showed a marked production of osteoid tissue and also the formation of trabeculae of normal, newly formed bone. The osteoid tissue arose from cells that had many of the features of osteoblasts. The tumor

has not recurred two years after operation, although on casual examination the histologic appearance suggests the diagnosis of osteogenic sarcoma. It is believed that this tumor is an osteoblastic, osteoid-forming tumor of slow growth, and that the prognosis is favorable. Early in the course of the growth a biopsy was made. The histologic pictures of the biopsy specimen and the surgically removed specimen are practically identical.

The only other report in which tumors of similar nature have been described is that of Bergstrand under the title of "Ueber eine eigenartige, wahrscheinlich bisher nicht beschriebene osteoblastische Krankheit in den langen Knochen der Hand und des Fusses" (*Acta radiol.* **11**:597, 1930).

JAFFE, New York. [ARCH. PATH.]

A CASE OF LYMPHATIC LEUKEMIA IN AN INFANT. R. R. STRUTHERS, Canad. M. A. J. **26**:209 (Feb.) 1932.

A case of lymphatic leukemia of four months' duration in an infant 16 months old is reported. The first symptoms noted were pallor, irritability and enlargement of the spleen and superficial lymph nodes. The blood picture showed severe anemia, slight leukocytosis, marked thrombocytopenia and the constant presence of myelocytes and reticulocytes in the peripheral blood.

An unusually large spleen, with evidence of severe focal necrosis, was found at autopsy. The liver also showed marked infiltration of white blood cells, chiefly of the large mononuclear, lymphocytic series. In places there were beginning abscesses. There was a marked degree of pachymeningitis externa.

MOORE, Omaha.

HYPERPITUITARISM BEGINNING IN INFANCY. L. H. BEHRENS and D. P. BARR, Endocrinology **16**:120 (March-April) 1932.

Giants over 7 feet (213 cm.) tall are extremely uncommon. Usually, if not always, they exhibit disturbed function of the pituitary gland as an etiologic factor, and there is delayed closure of the epiphyses. The abnormality usually begins at puberty, but in the case reported here the patient had grown abnormally and continuously from birth.

At birth he weighed 9 pounds (4,100 Gm.); at 6 months, 30 pounds (13,600 Gm.), and at 18 months, 62 pounds (27,200 Gm.); at 9 years he was 6 feet 1 inch (185.4 cm.) in height and weighed 178 pounds (80,700 Gm.).

When first seen, at 12 years of age, he was 208 cm. in height, and at 13 years he was 221.5 cm. He had had headaches, which had been corrected by glasses. He had always drunk large quantities of water. His appetite was vigorous. He was a good student and physically strong. Roentgenograms revealed a moderate tendency to prognathic development and an extraordinary development of pneumatic structure in the mastoid cells. The sella turcica was of extreme size, measuring 2.5 cm. in its anteroposterior diameter, and it was thought there was evidence also of a persistent Rathke's pouch. The genitalia were somewhat underdeveloped. Except for the enormous size of the sella turcica, local signs of pituitary involvement were almost entirely lacking.

Of especial interest in this case are: (1) the beginning of the abnormal development in early infancy, (2) the low basal metabolic rate accompanied by subnormal temperature and cold hands and feet and (3) the extraordinary size of the mastoid cells and the pneumatization of the squamous portion of the temporal bone.

JACOBSEN, Buffalo.

DISTRIBUTION AND IMPORTANCE OF PAPER MULBERRY (PEPYRIUS PAPYRIFERA KNUTZE) AS A CAUSE OF HAY-FEVER AND ASTHMA IN THE UNITED STATES. R. M. BALYEAT and H. J. RINKEL, J. Allergy **3**:7 (Nov.) 1931.

A description is given of the paper mulberry tree which produces a large amount of toxic pollen in the latter part of April and the first part of May. The

pollen causes hay fever and asthma in sensitive persons. The authors have found eighteen persons sensitive to the pollen and have seen eleven patients with asthma and hay fever who were clinically sensitive to mulberry pollen.

A map shows the distribution to be chiefly in the southeastern part of the United States.

HOYER, Cincinnati.

GLUE SENSITIVITY. GEORGE C. ANDREWS and CHARLES W. MCNITT, J. Allergy **3**:30 (Nov.) 1931.

A case is reported of a patient sensitive to glue. The entrance of the patient into her art class or contact with stickers, labels or glue would produce asthmatic attacks or swelling of the tongue, lips or face. She was treated with a fish glue extract in gradually increasing doses, beginning with 2 minims (0.123 cc.) of 1:100,000 dilution. Her symptoms were completely relieved. Four subjects were passively sensitized with the patient's serum and reacted locally to glue, codfish protein and stickers. The properties and uses of fish glue are discussed.

HOYER, Cincinnati.

THE BIOLOGIC IDENTITY OF CERTAIN GRASS POLLEN CAUSING HAYFEVER. ARTHUR STULL, ROBERT A. COOKE and JAMES H. BARNARD, J. Allergy **3**: 351 (May) 1932.

Clinical and laboratory experiments were performed with the pollen of the following grasses: timothy (Phleum pratense), Bermuda (Cynodon-Capriola dactylon), Johnson (Sorghum halepensis), orchard (Dactylis glomerata), June (Poa pratensis), redtop (Agrostis palustris) and rye (Secale cereale). From these experiments, the authors conclude that the active substance of these pollens is a single substance and is common to all the extracts. A person who is sensitive to any one of these grasses may be treated successfully with the extract of timothy pollen.

HOYER, Cincinnati.

SERIAL SKIN TESTS AS A GUIDE IN THE TREATMENT OF HAYFEVER, PRELIMINARY REPORT. ABRAHAM COLMES, J. Allergy **3**:449 (July) 1932.

Serial tests of the skin were made on a group of 44 patients with hay fever who received preseasonal treatment. Tests of the skin were made at the beginning of treatment, after from eight to ten inoculations and at the end of the treatment. The reactions of the skin in these patients varied from 1 plus to 4 plus. There was a diminution in the reaction of the skin in 91 per cent, while 98 per cent of the patients showed some relief from the treatment. The relief varied from a slight improvement of symptoms to complete absence of symptoms. These results would indicate that the skin test could be used as a means of determining the number of doses needed to treat a patient successfully.

HOYER, Cincinnati.

EMANATION OF FLIES AS EXCITING CAUSES OF ALLERGIC CORYZA AND ASTHMA: V. A STUDY OF THE ATOPIC REAGINS OF THE CADDIS FLY, BUTTERFLY AND MOTH. SALVATORE J. PARLATO, J. Allergy **3**:459 (July) 1932.

A series of experiments was conducted with the blood of three patients who were sensitive to emanations of the butterfly, moth and caddis fly and of one patient with a reaction of the skin to the butterfly and moth, but not to the caddis fly. The atopic reagins of the serum of the persons sensitive to these flies are transferable to the skin of nonallergic persons. Cutaneous sites which were sensitized with this serum were hyposensitized but not desensitized by repeated skin tests of the related allergen.

The atopic reagin of the butterfly is identical to that of the moth and similar to that of the caddis fly.

HOYER, Cincinnati.

A Report of Six Cases of Flax Seed Sensitization with Review of the Literature. Lucile Ruffe Grant, J. Allergy **3**:469 (July) 1932.

The literature is reviewed fully and the cases therein reported are classified according to the location of the important symptoms, in the gastro-intestinal tract, the respiratory tract or the skin. A list of many articles in which flax seed is used is included.

Six patients with a positive cutaneous reaction to flax seed were found in a group of 111 patients. The six ranged in age from 8 to 54 years. Of five who were asthmatic, three obtained complete relief by avoiding contact with flax seed products, and another obtained complete relief with desensitization.

Hoyer, Cincinnati.

Calcinosis Universalis. Clifford G. Grulee, M. Clin. North America **16**:447 (Sept.) 1932.

A boy, 2½ years old, complained of pain in the left leg and of the presence of hard, tender lumps in the legs, arms and back. These symptoms had been present for one year. On palpation there could be felt beneath the skin numerous deep, hard, shotlike masses. They were rather symmetrically placed under the skin over the medial side of the upper arm, extending to the anterior margin of the axilla; they were also present over the inguinal ligament and the medial side of the thigh. The nodules decreased in size and number toward the knee, and were absent in the hands and feet. They were also present over the lower part of the trunk and were especially numerous about the buttocks and hips. Sections of a nodule revealed areas of dark-staining material impregnated with calcium and surrounded by fibrous connective tissue. Roentgen examination showed, besides the superficial nodules, deep-seated masses and shadows suggestive of incrustations along the sartorius muscles. Very little change was noted after eight months.

Smith, Ogden, Utah.

Ascites in Infants. Arthur F. Abt, M. Clin. North America **16**:507 (Sept.) 1932.

Transudation of fluid into the peritoneal cavity of infants may result from cardiac or renal insufficiency or from obstruction to the portal circulation due to causes within or without the liver. In syphilitic disease of the liver, the spirochete may occasionally be found in the ascitic fluid. Rarer causes are severe anemia, Banti's disease and mesenteric Hodgkin's disease. Ascites due to exudates occurs mainly in peritoneal inflammation, the result of infection with the tubercle bacillus or with pyogenic organisms. Fetal ascites may be due to fetal peritonitis or to portal obstruction caused by gummas of the liver or by circulatory abnormalities. General fetal dropsy is always accompanied by ascites. Abt reports a case of ascites occurring as a rather isolated symptom in an infant of 7 months. Syphilis and tuberculosis could be definitely ruled out. At autopsy the portal and splenic veins and the vena cava were found to be normal. There was found, however, a severe hepatitis, presumably of infectious origin, which undoubtedly gave rise to the ascites.

Smith, Ogden, Utah.

Acute Upper Respiratory Infection in Infants and Children. Samuel A. Cohen, M. J. & Rec. **135**:1 (Jan. 6) 1932.

Infections of the upper respiratory tract appear to be more frequent in localities where there are sudden changes in temperature. This infection is the most frequent single acute disease confronting the clinician today. Some infants and children seem to be more predisposed to such infections than others. Children suffering from rickets and those undernourished are especially predisposed.

The bacteriology of these infections is discussed next, and signs found on physical examination are given in detail. The commonest complications are otitis media, from which may follow acute mastoiditis, conjunctivitis, stomatitis and

bronchopneumonia. One troublesome symptom is the abdominal pain so often met with in these cases of nasopharyngitis. This is generally a colic-like pain and centers around the umbilicus. Usually marked rigidity is absent, but one must always bear in mind the differential diagnosis of this condition and appendicitis. The reactions of acute infections of the upper respiratory tract and rheumatic fever open up many avenues of speculation. The fact that the peak of occurrence of rheumatic fever is reached during the same period as that of infection of the upper respiratory tract is more than suggestive of the close relationship existing between these two diseases. These infections can be reduced by paying more attention to such factors as ventilation, avoidance of wet feet and clothing.

WILLIAMSON, New Orleans.

VETERINARY ASPECTS OF UNDULANT FEVER. J. F. DE VINE, New York State J. Med. **31**:1255 (Oct. 15) 1931.

In some portions of New York State 20 per cent of the raw milk examined was infected with Bacillus abortus. In one infected herd, 75 per cent of the animals excreted Bacillus abortus from one or more quarters.

Pasteurization of milk offers the best protection against undulant fever.

AIKMAN, Rochester, N. Y.

EXOPHTHALMIC GOITRE IN CHILDREN. GEORGE E. BEILBY and JAMES G. CARLTON, New York State J. Med. **31**:1329 (Nov. 1) 1931.

In a series of 1,600 cases of exophthalmic goiter 5 occurred before puberty. The ages of these children were 2 years and 9 months, 9 years, 11 years, 11 years and 13 years. Between 13 and 15 years a larger number was found.

The author believes that the same principles should govern the surgeon in the treatment of these patients as in that of the adult. The complete operation was done in every instance. Slightly larger amounts of the gland should be left behind in children. A longer period of hospitalization is advised. Of the 5 patients whose cases are reported 3 have remained well, and 1 had a slight recurrence. The first case is of too recent date to determine the final outcome. The child, 2 years and 9 months of age, was up and about the ward one week after the operation and all symptoms had disappeared.

AIKMAN, Rochester, N. Y.

PURULENT PERICARDITIS: A REPORT OF SEVEN CASES. RICHARD JOSEPH WHITE, South. M. J. **25**:364 (April) 1932.

The author believes that half of the cases of purulent pericarditis could be saved if the patients were properly treated. The majority of the cases seen complicate pneumonia; some of them follow empyema. In some of the cases osteomyelitis has been the original lesion. The author's cases afford examples of all these conditions.

Precordial edema is often seen in children affected with this disorder. Aspiration should always be performed when the condition is suspected. In aspirating, three things must be considered: (1) the safety of the heart, (2) possible injury to the internal mammary artery and (3) accidental contamination of the pleura. In the seven cases reported by the author, six of the patients made complete recoveries, and only one died.

SCHLUTZ, Chicago.

CARBON DIOXIDE IN THE TREATMENT OF ACUTE BRONCHITIS AND EARLY PNEUMONIA. JAMES F. ALISON, South. M. J. **25**:386 (April) 1932.

The author reports a series of cases of acute bronchitis and early pneumonia occurring in very young infants and children treated by the administration of a combination of carbon dioxide and oxygen.

The usual concentration was 5 per cent carbon dioxide and 95 per cent oxygen. The treatment did not seem to affect the length of the illness materially, but the

patients were more comfortable, had less cyanosis and appeared to progress better than patients who received plain oxygen.

The author reports it as a valuable adjunct to the treatment of acute bronchitis and early pneumonia. He reports pneumonia as a "pneumococcic atelectasis"—a conception formulated by Coryllos and Birnbaum.

In some of the cases the treatment seemed to be almost abortive.

SCHLUTZ, Chicago.

LYMPHOCYTIC LEUKEMIA CAUSING PONTILE HEMORRHAGE. J. C. HAWKSLEY, Arch. Dis. Childhood **7**:29 (Feb.) 1932.

A girl of 10 years had been limping slightly for three days. Suddenly there was paralysis of the entire left side. A diagnosis of lymphocytic leukemia was made, with hemorrhage in the internal capsule or pons. At autopsy hemorrhage was found in the pons. Microscopic examination of the pons showed it to be heavily infiltrated with lymphocytes around the area of hemorrhage.

The nervous manifestations of leukemia in this case were due to lymphocytic infiltration of the pons, followed by hemorrhage.

KELLY, Milwaukee.

TUMOR OF THE SUPRARENAL CORTEX IN AN INFANT OF EIGHTEEN WEEKS. REGINALD LIGHTWOOD, Arch. Dis. Childhood **7**:35 (Feb.) 1932.

A male infant of 18 weeks presented a tumor of the left suprarenal cortex as large as the kidney, described as benign cortical adenoma. When this infant was 11 weeks old, a diffuse fatty swelling developed over the back and neck. The chin and cheeks became enlarged, and there was an abnormal hairiness of the forehead.

KELLY, Milwaukee.

MYOSITIS OSSIFICANS PROGRESSIVA. WILLIAM F. MAIR, Edinburgh M. J. **39**:13 (Jan.); 69 (Feb.) 1932.

The thesis of Mair, roentgenologist at the James Mackenzie Institute for Clinical Research, St. Andrews, with an addition from recent Japanese and Italian pathologic studies, is found in two numbers of the *Edinburgh Medical Journal*. Mair's two cases of this rare disease have given no opportunity for a pathologic study of material. Therefore the researches of Ipponsugi, of Tokyo, published in German, are drawn on for the findings in the muscles in a most painstaking study. No extensive British review or monograph had ever appeared, although a complete consideration of the subject in English was published by Rosenstirn of San Francisco in 1918.

The condition has only an antenatal or embryonic origin. The title is not entirely descriptive, for, as Greig has emphasized, muscle cannot change into bone, there being an intermuscular ossification of the fascia. Fibrous tissue, ligaments and muscle tendons participate in this transformation; the name, therefore, should be changed from myositis to fibrositis ossificans propressiva.

Mair does not deal with the traumatic or circumscribed forms of the disease. The incidence is rare. Only three cases have been traced in the British Isle, including the author's two cases. None are known in the great cities of London, Glasgow and Edinburgh at the present time. Instances have been reported from most countries, including five from the United States.

The disease shows a predilection for boys; it is found usually at birth or in early childhood, and it may be hereditary. The relation to rheumatic infection is difficult to prove, but seems to have been believed to exist by some writers. Its connection with epilepsy or imbecility has been reported in a few instances. Trauma has been present at birth in some of the cases, but apparently only as a factor that determines the site at which the lesion will develop in a person already having the possibility of such abnormal bone formation. Some of these children are born with congenital deformities, which fact seems to mean that

"susceptibility" exists to ossification of the tissues. Infections are not known to be a causal influence.

There appear at varying intervals swellings of different consistency, from soft cystlike to bonelike hardness. Some may have been present at birth or shortly afterward. These growths do not need to be symmetrical. They may change shape in the active or early stages, and give the false appearance of moving from place to place. Numerous swellings may appear at about the same time or finally. There seem to be remissions. The resultant swelling is bony-hard, and the overlying skin movable, though the skin may become ulcerated by the hard material that presses upon it. White chalky débris may be discharged, followed by healing. Lesions may disappear. Generalized ossification of the interstitial fibrous tissue within a muscle destroys the function and causes deformities.

The striped musculature of the body may become the seat of lesions, usually starting in the cervical spinal region and the shoulders. The sternomastoid or the temporomandibular muscles and the region of the ear are also usual sites. The back of the trunk is a favorite region. The heart, diaphragm, larynx, tongue, sphincters and muscles of facial expression fortunately are never involved.

There is generally no fever of any degree in this disease. The general symptoms are not so severe as one would expect. The children are happy, but at times uncomfortable from the lumps on the back. They are thin, and the unaffected muscles are atrophic. Early, however, the general health is not much affected. Complications may develop from the presence of the hard lumps or from infection, which is made easy by the immobility of the affected regions. Difficulty in swallowing and in respiration may arise.

Mair's two patients were children, a boy of 4 and a girl of 4½ years. Photographs are presented. The development of lesions and the general course of the disease are detailed. The girl died of pneumonia at about 5½ years of age.

The occurrence of this lesion on the head of a new-born infant might be confused with a cephalematoma, but the latter is usually limited to the parietal bone. If there is coexistence of sternomastoid lesions and cephalematoma in the first week of life the confusion is still greater.

Myositis fibrosa is sometimes difficult to exclude. It usually begins in the lower limbs, and is more common in girls. The limbs may be contracted; pain is a prominent symptom, and there is a tendency to recovery.

Multiple exostoses have a fine point of attachment to the body skeleton.

Pott's disease is hard to differentiate clinically from this condition except by the characteristic sites of each.

The prognosis is grave. Seldom does the patient reach adult life. A certain amount of spontaneous improvement sometimes occurs. No treatment is of curative benefit.

The author, in conclusion, states that the disorder is one of calcium metabolism. It is obscure in its mechanisms. There is a primary abnormality of development in which the potential function of osteogenesis has been impressed on all the connective tissue structures of the mesenchyma.

There are several pages of references to the modern literature.

NEFF, Kansas City, Mo.

GOITRE PROPHYLAXIS. KERTH D. FAIRLEY, M. J. Australia **2**:681 (Nov. 28) 1931.

The author's conclusions are: 1. Of all known diseases, simple goiter is the easiest and cheapest to prevent. 2. Its prevention would have beneficial effects on many related disorders. 3. Iodized salt of a strength of 1 part of potassium iodide in 250,000 parts of salt is an effective and safe prophylactic for general use. 4. If prophylaxis is limited to the school population, the ingestion of 5 mg. of iodine every week is effective and has no harmful effects. 5. The use of prophylactic measures during pregnancy is of the utmost importance. 6. The

individual practitioner can play a most effective part in the prophylaxis of goiter. 7. Simple goiter is, however, sufficiently common in certain parts of Australia to demand that the health authorities take steps to institute appropriate prophylactic measures.

GONCE, Madison, Wis.

PYELONEPHRITIS DUE TO THE PNEUMOBACILLUS OF FRIEDLÄNDER. BERTRAND-FONTAINE and R. PARLIER, Arch. de méd. d. enf. **35**:217 (April) 1932.

The authors report a severe case of pyelonephritis in a girl of 5 years, following a brief attack of rhinopharyngitis complicated with right otitis media. Nine days after the onset of otitis the child complained of sharp pains in the right flank; there were moderate temperature and rigidity. The following day these symptoms had disappeared, but the right kidney was palpable and somewhat mobile, and examination of the urine revealed pus containing not only staphylococci but also great numbers of encapsulated gram-negative diplococci. Cultures demonstrated the latter organism to be the pneumobacillus of Friedländer. Complete recovery occurred in a month.

Suppurative lesions of the kidney occasioned by this organism are exceedingly rare. Netter, Landstein, Wehring, Ribadeau-Dumas and Chabrun have reported such instances, all occurring in the course of a generalized septicemia.

AMESSE, Denver.

A CASE OF SODOKU OF THE LIDS. MONTHUS, FAVORY and LEVADITI, Arch. d'opht. **48**:493 (July) 1931.

The case of a child, 1 year old, with a rat-bite of the lid is reported. No organisms were found after a careful search. Death occurred notwithstanding the prolonged use of arsenicals. The fatal outcome of this case the authors attribute to the location of the initial lesions and the poor resistance of the patient. The characteristic clinical picture of sodoku includes an incubation period of from fifteen to twenty days (reduced to five or six in the severe cases). A more or less tender red swelling occurs at the site of the bite. When this swelling is incised, only a serosanguineous fluid escapes. Neighboring lymph glands are swollen. The temperature is elevated, but subsides when the localized swelling diminishes. General symptoms may appear which sometimes resemble measles. The disease lasts from two to three months before cure ensues. The mortality is between 6 and 12 per cent. The infective organism, a spirillum, is rarely found in the blood. The Wassermann reaction is almost always positive, and arsenical treatment usually beneficial.

Sodoku of the lid is rare, the lower extremities and hands being the common sites of the initial lesion.

MARLOW, Syracuse, N. Y. [ARCH. OPHTH.]

TREATMENT OF BRONCHOPNEUMONIA OF INFANCY. P. LEREBOULLET, Paris méd **1**:76 (Jan. 23) 1932.

The author considers the hygienic measures to be isolation and warm, moist air. Nasal antiseptics are the silver preparations and eucalyptol. Respiratory medications are turpentine and ammonium acetate. For the temperature, quinine and antipyrine may be given. If the circulation fails, camphor, caffeine or epinephrine hydrochloride may be used. Breast milk should be given occasionally, and dextrose solution for a tonic. Some forms respond to oxygen or oil of eucalyptus. Antipneumococcic or antistreptococcic serum may be used. Either autogenous or stock vaccines may be of value.

SANFORD, Chicago.

ROENTGENOLOGIC STUDY OF INTERLOBAR INFLAMMATIONS. M. PÉHU and J. BOUCOMONT, Rev. franç. de pédiat. **7**:342 (Oct.) 1932.

This study deals in particular with a type of interlobar inflammation which is plastic and adherent. The authors have called these lesions *"scissurites."* They

are found in tuberculosis, bronchopneumonia, lobar pneumonia, bronchiectasis and cardiac conditions. In infants they may frequently account for cases of obscure fever of long duration.

SANFORD, Chicago.

PUBERTY AND PRECOCIOUS MENSTRUATION. A. SEMENTINI, Prat. pediat. **10**:309 (July) 1932.

Following an attack of malarial infection with convulsions at the age of 14 months, a baby began to show precocious mammary and external genital development and to have monthly hemorrhages from the vagina, the hemorrhages lasting three to four days and being associated with irritability. The child was 2 years old at the time of the report. Dr. Sementini speculates on the possibility of a midbrain lesion as the cause of these changes.

DOOLEY, Kent, Conn.

PYELOCYSTITIS IN INFANCY WITH PARTICULAR REGARD TO TREATMENT. G. B. CAVALLO, Prat. pediat. **10**:339 (Aug.) 1932.

The entire issue of *La pratica pediatrica* for August is devoted to Dr. Cavallo's exhaustive review of the literature on infantile pyelocystitis. The bibliography includes sixty articles, about one half of which are in Italian, but unfortunately covers very little work published in the last five years.

DOOLEY, Kent, Conn.

TWO CASES OF BACILLUS COLI ORCHIEPIDIDYMITIS. R. COTA, Prat. pediat. **10**:409 (Sept.) 1932.

The first case was that of a boy, aged 5 years, in whom an acute attack of fever, vomiting and diarrhea developed; he was found to have pyuria on the fourth day. Bacillus coli was present in the urinary sediment and was recovered from cultures. About five days after the discovery of the pyuria, the child began to have pain and swelling in the right testis and epididymis. He was treated with an autogenous vaccine and methenamine, and made a complete recovery.

The second case was that of a man, aged 24, who had a sudden onset of fever, diarrhea and lumbar pain; he was found to have pyuria due to Bacillus coli. On the twelfth day acute epididymitis and orchitis developed. Without specific treatment, he made a complete recovery.

The author adds a brief review of the literature and a discussion of the differential diagnosis.

DOOLEY, Kent, Conn.

A CASE OF UNCOMPLICATED CONGENITAL AORTIC STENOSIS. H. MÜLLER, JR., Schweiz. med. Wchnschr. **62**:162 (Feb. 13) 1932.

The case of a young man, normally developed, had been diagnosed as aortic stenosis in early childhood, and he was kept under regular observation. His heart showed a loud sharp blowing systolic murmur, loudest in the first and second right intercostal spaces, and transmitted into the vessels of the neck. The second aortic sound was accentuated. The first sound at the apex was doubled. There was a heaving precordial impulse, and the pulse was feeble. Roentgenograms showed a hypertrophied left ventricle and broad aortic shadow. There were never any symptoms; death occurred suddenly following unusual exertion. Autopsy gave negative results except for the heart. The left ventricle was markedly hypertrophied, and the ascending aorta somewhat dilated. The aortic leaflets were fused, stenosing the orifice. There were no associated cardiac anomalies or inflammatory changes. Microscopically, the aortic leaflets were scarred and fibrotic. The lesion was attributed to fetal endocarditis. The author states that the prognosis for health and duration of life is much more favorable in the uncomplicated cases of congenital aortic stenosis than in those accompanied by other anatomic defects.

WOLMAN, Chicago.

PNEUMOCOCCIC SEPTICEMIA WITH AN UNUSUAL LOCALIZATION. J. C. NAVARRO and A. F. AJA, Arch. argent. de pediat. **2**:365 (July) 1931.

The authors report the case of a girl 6 years old who a month before admission began to develop insidiously generalized edema and oligemia, not severe enough, however, to confine her to bed. Two days before admission to the hospital, chills and fever, with all other signs and symptoms of severe infection, suddenly developed.

The physical examination at the time of admission revealed an acutely ill child with generalized edema, severe abdominal symptoms suggestive of peritonitis and erysipeloid areas on the back and abdomen, which a week later developed into extensive cellulitis. The analysis of the urine revealed extensive albuminuria and cylindruria and only an occasional erythrocyte. The cellulitis continued to become more and more diffuse until most of the subcutaneous edematous fluid became hemorrhagic and purulent.

The skin itself remained practically unaffected except over the erysipeloid areas described, which appeared earlier in the disease. The purulent material obtained from the subcutaneous abscesses as well as from the purulent edematous fluid contained a pure culture of a pneumococcus. The child died three weeks after admission, in a state of a severe toxemia.

The authors point out the absence in this case of pneumonia and of involvement of serous membranes, which frequently occurs in pneumococcic septicemias, with the unusual involvement of the subcutaneous edematous tissue by a suppurative process.

SCHLUTZ, Chicago.

TREATMENT OF EXUDATIVE PLEURISY IN CHILDREN. A. J. CHURA, Med. Klin. **27**:1858 (Dec. 18) 1931.

In cases of nonpurulent exudative pleurisy the author has seen good results from medication with from 0.5 to 1 Gm. of sodium salicylate occasionally combined with sodium bicarbonate. Also calcium and theobromine sodiosalicylate have been given from three to five times a day in doses of 0.3 Gm. At the same time vitamins were supplied in sufficient amounts. The author believes that with such treatment the average duration of the disease has been considerably cut down.

ZENTAY, St. Louis.

TREATMENT OF ANEMIA WITH LARGE DOSES OF METALLIC IRON. GUSTAF LINDBERG, Hygiea **93**:529 (July 31) 1931.

The author reviews the pharmacology of iron therapy, stressing the view that the effect of iron is stimulation of the hematopoietic system rather than a replenishment of body iron. He advises the administration of from 1.5 to 3 Gm. of the reduced or powdered iron per day before meals in powdered form. No intolerance or tendency to constipation was noted. The hemoglobin and erythrocytes increased remarkably within the first week of administration. The blood picture generally showed marked regeneration.

ELGHAMMER, Chicago.

GAUCHER'S DISEASE. H. G. K. WESTENBRINK, Nederl. tijdschr. v. geneesk. **75**:4983 (Oct. 3) 1931.

The author made a chemical investigation of the spleen removed from one of the patients with Gaucher's disease, formerly described by de Lange (*Nederl. tijdschr. v. geneesk.* **75**:2037, 1931). Westenbrink compared his results with those of Epstein and Lorenz, who recently gave a survey of the chemical properties of the spleen in the three types of lipoidosis (Niemann-Pick's disease, Schüller-Christian's disease and morbus Gaucher). In agreement with the chemical properties given for the spleen in Gaucher's disease, the author found that the lecithin content showed nothing particular; the cholesterol content was rather high, but

could not be compared with the very high value found in Schüller-Christian's disease, and the very high amount of kerasin typical of Gaucher's disease (Epstein and Lieb) was present.

VAN CREVELD, Amsterdam, Holland.

LOCAL INFILTRATIONS AFTER INJECTION OF INSULIN. L. A. HULST, Nederl. tijdschr. v. geneesk. **75**:5278 (Oct. 24) 1931.

Infiltration around the site of injection was observed in four patients. These local reactions in each case appeared nine days after the beginning of the treatment. This hypersensitiveness exists sometimes for one and sometimes for more preparations. Usually it is easy to remove this disagreeable complication. Sometimes the temporary or constant use of another kind of insulin is sufficient. Often the hypersensitiveness disappears spontaneously. If there is hypersensitivity to several preparations of insulin, temporary interruption of the treatment may help. Possibly also desensitization produced by the giving of a number of intracutaneous injections of small amounts of insulin (Schill) may be of value. Local reactions thus rarely make it necessary to give up treatment with insulin.

VAN CREVELD, Amsterdam, Holland.

SO-CALLED CATARRHAL JAUNDICE. C. H. VERBOOM, Nederl. tijdschr. v. geneesk. **75**:5283 (Oct. 24) 1931.

Several cases of infectious hepatitis of increasing severity observed in children are reported. From these observations and from those reported in the literature the author concludes that, although the greater part of the patients suffering from this disease are only slightly ill, the possibility that infectious hepatitis may develop into acute yellow atrophy of the liver always exists. Moreover, the development of the condition into cirrhosis is possible. It is therefore recommended that patients with so-called catarrhal jaundice which lasts longer than two or three weeks be treated with small amounts of insulin and sugar and be given from the beginning a diet rich in carbohydrates and relatively poor in protein. A moderate amount of fat is not contraindicated as long as bile comes into the intestines, and probably is even helpful in increasing the resistance of the patient.

VAN CREVELD, Amsterdam, Holland.

OSTEOPETROSIS. E. S. FRANK, Nederl. tijdschr. v. geneesk. **75**:5794 (Nov. 28) 1931.

Osteopetrosis was described for the first time by Albers-Schönberg in 1904. The author describes three cases observed in children in one family who were born successively. The parents were healthy. The children born after the three who had osteopetrosis were in good health. Two of the sick children died. Splenectomy was performed on the third. The chief symptoms of the deceased children were found in the blood and in the bloodmaking apparatus. The third child presented, in addition to the changes in the bones characteristic of this disease, thickening of the periosteum of the long bones and the ribs, loss of teeth without perceptible disease of the jaws and an increased fragilitas globularis. The author gives the points of differential diagnosis between this condition and congenital hemolytic anemia, and presents objections to the opinion of Péhu, Policard and Dufourt (*Presse méd.* **39**:999, 1931), namely, that the primary disease is situated in the glandulae parathyroidales, on account of which they advise partial parathyroidectomy.

VAN CREVELD, Amsterdam, Holland.

Nervous Diseases

BRAIN ABSCESS (PARADOXICAL) IN CONGENITAL HEART DISEASE. MEYER A. RABINOWITZ, JOSEPH WEINSTEIN and ISRAEL H. MARCUS, Am. Heart J. **7**:790 (Aug.) 1932.

The authors recite the fact that this condition was recognized by the older English students. The first definite report is credited to Ballet in 1880. Up to

the present ten cases have been reported in the literature (which are analyzed in this paper), while the author's own case is given in detail. Further reference is also made to paradoxical cerebral emboli without an infective factor. It is quite clearly shown that a defect of the interventricular septum is present in all such cases, and that the condition is associated usually with the tetralogy of Fallot. The average age of death was 16½ years. Complete postmortem data are given in the reported case and a comprehensive discussion follows.

BACHMANN, Chicago.

CARDIO-RESPIRATORY VARIATIONS IN PERSONALITY STUDIES. J. A. LARSON and G. W. HANEY, Am. J. Psychiat. **11**:1035 (May) 1932.

Cardiorespiratory tracings by the polygraph method may be of distinct aid in the study of delinquencies, and are particularly adaptable to problems of child behavior in which freudian analysis may be contraindicated. Protocols based on a study of 235 children are presented. This procedure may prove to be of definite value to the psychiatrist either in corroborating or in the clearing of the following classes of cases: (1) false accusations made by juveniles against adults, involving sexual charges. at times made at suggestion from others or through motivations; (2) malingering in any form; (3) elimination of children wrongfully accused of delinquency; (4) when it is necessary to secure a reliable sex history; (5) in probing for complexes when support cannot be attained.

Detailed description of the principles involved and methods for procedure and interpretation of results are given.

JAHR, Omaha.

AUDITORY HALLUCINATIONS IN "NONPSYCHOTIC" CHILDREN. MAX LEVIN, Am. J. Psychiat. **11**:1119 (May) 1932.

Four boys were studied in the psychiatric department of the Community Health Center at Philadelphia. All of them presented auditory hallucinations with varying frequency. The age of onset was 1½ years in case 1, 10 years in case 2, 7 or 8 years in case 3 and 14½ years in case 4. The duration of the condition in case 1 was eight months; that in case 2, ten months; that in case 3, from three to four years, and that in case 4, indefinite.

Study of the etiology revealed that the chief factor in the home was poverty; all four boys came from social agency homes. Family crises, desertion, cruelty, death of a parent, low general intelligence (consciousness of a deficit) and problems of personality were determined to be the principal etiologic elements.

The perceptual quality of the hallucinations was described as follows: "My mind tells me." "I hear a voice." "My heart tells me." "It's like a teeny voice inside." "It sounds quiet, like if you're whispering in somebody's ear." The localization was given as the left ear, the right ear, the heart and the head. The content was a complete sentence always given in the imperative mood, at times expressing conflicting demands.

The author interprets the hallucinations as functions of defense, enhancement of self-esteem, satisfaction of instinctive cravings and of desire for pleasure, repression of unwelcome cravings and expiation of a sense of guilt. The treatment consists of sociologic adjustment which tends to obviate the sense of insecurity on the part of the child.

JAHR, Omaha.

THE DEMENTIA PRAECOX CHILD. WINIFRED RICHMOND, Am. J. Psychiat. **11**:1153 (May) 1932.

Kraepelin is quoted as stating that 7 per cent of his patients with dementia praecox had always been "weakminded." It is only recently that with the development of the child guidance clinics the unusual child has become the object of special personality studies. The present status is not ideal. The psychiatrist

knows little psychology, and the psychologist is ignorant of psychiatry. A type of child which is frequently found in the history of the praecox case is the child with behavior problems. He may be incorrigible in the literal sense of the word, engaging in cruel and senseless conduct which is inflexible. He seldom makes social contacts. He is the "queer," the "different" child in the family. Reality is shunned, and the youngster flits out of one difficulty into another. His school work is poor, though not necessarily because of mental deficiency. Because he does not apply himself and does not train his mental aptitudes, he may give one the impression of feeblemindedness. With this lack of training his mental faculties are materially reduced in time, and in later years he becomes a part of the horde of ne'er-do-wells. At times in desperation he becomes a big-hearted hero, and giving vent to the spirit of adventure, he may join the army or navy only to be entirely crushed under regulation and discipline. He now becomes a true psychotic type.

JAHR, Omaha.

A CONTRIBUTION TO THE EARLY DEVELOPMENT OF THE EGO. L. P. CLARK, Am. J. Psychiat. **11**:1161 (May) 1932.

A detailed psychologic study is made of the relationship between the life instinct and the death instinct based on freudian conceptions of the ego.

JAHR, Omaha.

TRAUMATIC INTRACRANIAL HEMORRHAGE WITH RECOVERY IN AN INFANT FIVE MONTHS OF AGE. EDWARD LEWIS and WILLIAM SILVERMAN, Arch. Pediat. **49**:479 (July) 1932.

A case of traumatic intracranial hemorrhage in an infant 5 months of age, with recovery, is reported. In spite of the extensive intracranial involvement, the only external evidence of trauma was a small ecchymotic spot on the right cheek. In the absence of any definite localizing symptoms, the case must be considered one of severe concussion with multiple small cortical and retinal hemorrhages, rather than a large hemorrhage from a ruptured vessel. At the time of discharge, there was no evidence of residual damage to the brain, the eyes or elsewhere.

AUTHOR'S SUMMARY.

CAN BIRTH CONTROL REDUCE INSANITY? H. A. COTTON, Birth Control Rev. **16**:12 (Jan.) 1932.

Five hundred cases of so-called functional types of mental disorders were analyzed by the author in relation to the order of birth. The following startling facts were deduced from the tabulation of the data. "Cases in which the patient was the only child amounted to only 19, while the first child was found to be insane in only 65 cases. Thus only 5 per cent of the number were only children and only 23 per cent of this group including the only child were the first children. In other words, 77 per cent of the cases occurred in children who were born after the first child." Relying on such data as this, Dr. Cotton later states: "In view of these facts it appears to me that if we cannot make any inroads on the increasing ratio of insanity by other methods, that birth control offers a very sure method of decreasing the number of insane patients admitted to the institutions." A glance at the amateurish statistical methods used in this paper shows that there are numerous obvious fallacies. In the opinion of the reviewer the number of cases used is not large enough, nor uniform enough to allow of statistical treatment. The table really proves nothing and certainly does not justify the conclusions quoted. Such misleading deductions published in a magazine the object of which is obviously propaganda do harm to the cause of psychiatry.

COBB, Boston. [ARCH. NEUROL. & PSYCHIAT.]

BLOOD GROUPING IN POLIOMYELITIS: THE RELATION TO SUSCEPTIBILITY AND THE NEUTRALIZING PROPERTY OF CONVALESCENT SERA. C. W. JUNGEBLUT and L. W. SMITH, J. Immunol. **23**:35 (July) 1932.

To shed further light on various constitutional factors that might influence susceptibility to poliomyelitis, the authors studied the distribution of blood groups in patients who had or who had had poliomyelitis.

In patients under 5 years of age there was no marked deviation from the normal figures. Above this age, there was a distinct diminution in group B and a slight increased in group O. This shift in distribution became progressively more marked with advance in the age of the patient at the onset of the disease. There was a predominance of deaths in the A group between the ages of 5 and 10 years, and in the O group after the age of 10 years.

Six of seven specimens of serum from convalescent patients with the B type of blood were capable of neutralizing the virus of poliomyelitis in vitro; whereas, only one third of six specimens of A serum and one half of thirteen specimens of serums from convalescent patients of groups O and AB possessed this property.

FOTHERGILL, Boston.

PARENTAL ATTITUDES AND MENTAL HYGIENE STANDARDS. RALPH STOGDILL, Ment. Hyg. **15**:813 (Oct.) 1931.

In order to compare parental standards of child behavior with the outlook of mental hygienists on the same subjects, Stogdill prepared a list of seventy items of behavior and submitted it to a large group of parents. They were told to indicate the gravity or desirability of each by a number on a scale, the rating 1 indicating "of no consequence," the number 5 meaning "undesirable" and the symbol 10 meaning "very serious." Intermediate ratings were indicated by intervening numbers. A similar questionnaire was submitted to a group of mental hygienists. The items rated most serious by the parents were: stealing, masturbation, lying, cheating and disobedience, in the order given. Mental hygienists, on the other hand, considered depression, fears, cruelty, whining and suspicion the most undesirable traits. Among the qualities assessed by the parents as being of little or no consequence were: shyness, imaginative story-telling, bashfulness, make-believe daydreaming and excessive reading. Significant items on which these groups differed widely were: modesty, suspicion, bashfulness, seclusiveness, sulkiness and sensitiveness — all of which were much more serious to psychiatrists than to the parents. On the other hand, swearing, defiance, smoking, masturbation and engaging in obscene talk were taken much more seriously by the fathers and mothers than by the mental hygienists. It would appear that parents regard transgressions against morality, opposition to parental control, disrupting the routine of the household and breaches of etiquet serious items of child misbehavior, whereas mental hygienists are inclined to emphasize introverted reactions and seclusive attitudes. Since child guidance should be primarily, or at least, ideally, a parental function, the fathers and mothers must be educated to more sound standards of physically hygienic behavior.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

TWO CASES OF LINDAU'S DISEASE: ANGIOMA OF THE CEREBELLUM IN THE MOTHER AND VON HIPPEL'S DISEASE IN THE SON. E. HARTMANN and G. SOURDILLE, Ann. d'ocul. **168**:881 (Nov.) 1931.

Cases of angioma of the cerebellum in a mother associated with Lindau's disease and of angiomatosis retinae (von Hippel's disease) in her son are reported by Hartmann and Sourdille. The authors point to the association of these two diseases, which are often found in the same patient, as further evidence of the close relation between the brain and the eye which is evident from anatomic, histologic and embryologic studies. They believe that these cases point to the

familial character of Lindau's disease, and urge careful examination of the periphery of the fundus in patients who are suspected of having cerebral tumors.

BERENS, New York. [ARCH. NEUROL. & PSYCHIAT.]

THE RECOGNITION OF THE OPERATION OF CHANCE BY THE CHILD. MARGUERITE LOOSLI-USTERI, Arch. de psychol. **23**:45 (April) 1931.

In a continuation of her studies on the Rorschach test, the author has made some interesting observations on the capacity of the child to recognize the operation of chance as a causal phenomenon. Piaget has stated that this recognition does not exist in the child of 7 or 8 years, but the author finds such a capacity undeveloped in the child between the ages of 10 and 13 years. The absence of this capacity is associated with the absence of any attempt to interpret the Rorschach figures. Such an absence is not surprising, because the capacity to recognize the action of chance cannot exist until there is some recognition of the laws of cause and effect. In this the young child resembles the primitive man. The recognition of the operation of chance as a causative factor occurs as the child begins to abandon his egocentricity—an important step in his development. The resistance maintained by young children against the recognition of the possibility of chance as a causal phenomenon indicates that the child really desires not to acknowledge such a possibility because to recognize its existence is to acknowledge that reality may be different from fantasied reality, and thus to admit the possibility of doubt. It would seem that the recognition of the causal activity of chance occurs at the same time that the child is willing to entertain doubts as to the validity of the concepts he has accepted up to this time, and that both of these phenomena develop at the beginning of adolescence. Many, if not most, adults also show traces of resistance to this concept and oppose the destruction of their infantile world through occultism, mysticism, religion, etc. This article is extremely interesting and well worth reading in the original.

PEARSON, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

TECHNIC OF TREATMENT OF CHILDREN BY SUGGESTION. FRANZ HAMBURGER, Arch. f. Kinderh. **97**:129 (Sept. 9) 1932.

Excellent results may be obtained in treating children by employing the power of suggestion. It is necessary that neither the child nor the mother suspects that this method is being used. Confidence in the physician is essential for the success of suggestion therapy. The physician may use medicine, local applications, electrical treatments, etc., and the patient is assured that in a given time certain results will follow. The effectiveness of this treatment depends on the manner in which the physician handles the patient. The author mentions chronic cough, pavor nocturnus, tic and enuresis as conditions amenable to treatment by suggestion, and gives rather detailed instructions for the proper management. He believes that the principles of suggestion should be used much more by pediatricians.

LEMASTER, Evanston, Ill.

DEVIATION OF THE BODY AND THE GAIT IN CEREBELLAR DISEASE. H. HOFF and O. PÖTZL, Jahrb. f. Psychiat. u. Neurol. **48**:217, 1932.

The authors report a case of cerebellar syndrome following apoplexy due to hypertension. Early in the disease there were forced rotation to the right (with the body in the upright position) and, later, deviation of the head and body to the right while standing or walking. Only in this position were the equilibratory disturbances (vertigo and falling to the right) compensated for. Necropsy revealed a softening in the right cerebellar hemisphere limited exclusively to the white substance; the lesion extended laterad from the dentate nucleus, its greatest diameter being in the sagittal plane. The cerebellar cortex was intact, only a narrow zone in the most lateral portion of the dentate nucleus being somewhat

affected. The clinical picture of cerebellar deviation in this case is attributed to the supranuclear softening in the right cerebellar hemisphere, in contrast to the usual clinical picture consisting predominantly of hypotonia, tremor, dysmetria and cerebellar ataxia of certain muscles of the upper extremities noted in cases of softening of the hilus of the dentate nucleus. In the case reported there was an interference with the function of the lateral portion of the right dentate nucleus, whose primary clinical manifestations were disturbances in equilibrium of the body toward the side of the lesion. These disturbances were in evidence only during gait, with the body in the upright position. They were otherwise analogous to the forced rotations of the body (rolling phenomena) observed in quadrupeds following hemicerebellar extirpation.

KESCHNER, New York. [ARCH. NEUROL. & PSYCHIAT.]

MOTOR ELEMENTS IN AGRAPHIA (DISTURBANCES OF WRITING AND FORCED GRASPING). L. BOUMAN and A. A. GRÜNBAUM, Monatschr. f. Psychiat. u. Neurol. **77**:223 (Nov.) 1930.

The generally accepted conception of agraphia does not include disturbances of writing caused by purely motor defects. Nevertheless, the authors believe that careful examination of patients with agraphia will reveal motor disorders of a compulsive nature. In support of their view, a detailed investigation of a case is reported. It was that of a patient with cerebrospinal syphilis who showed signs of multiple lesions of the brain. One of the most prominent features of the clinical picture was complete agraphia. The usual tests of motor function of the fingers of the right hand yielded normal results. By the use of block letters, however, the following abnormalities were brought out: compulsive turning of the hand toward the object observed and forced grasping of objects that stimulated the sense of touch in the hand. These disturbances led to difficulty in forming letters, for as soon as the fingers touched the paper they tended to cling to one spot. The increased effort necessary to overcome this resulted in the production of heavy strokes. Furthermore, the first letter acted as a visual stimulus which hindered the hand from moving onward. Consequently, there was a marked tendency for succeeding letters to encroach on the space occupied by previous letters. At times the writing of the patient showed motor perseveration. This owed its origin to the fact that the compulsive phenomena could be overcome only by impulses that were so strong that they frequently caused a repetition of the required motor act.

In order to test the validity of the view that agraphia may be based on compulsive motor phenomena, the authors investigated a case of encephalitis in which forced grasping was a prominent symptom. The examination was undertaken only when the compulsive symptoms were beginning to disappear. The handwriting of the patient then showed changes similar to those found in the first case. Furthermore, it closely resembled the writing of a patient reported by Erbsloh to have isolated agraphia. According to Bouman and Grünbaum, a careful analysis of many of the symptoms described by other authors in cases of agraphia indicates that these symptoms are produced by purely motor phenomena of a compulsive nature.

ROTHSCHILD, Foxborough, Mass. [ARCH. NEUROL. & PSYCHIAT.]

THE RÔLE OF THE CHOROID PLEXUS IN THE FORMATION OF THE CEREBROSPINAL FLUID. B. PURJESZ, M. DANCZ and K. HORVÁTH, Monatschr. f. Psychiat. u. Neurol. **77**:319 (Dec.) 1930.

Investigation of the changes produced in dogs by toxic substances, such as corrosive mercuric chloride, uranium nitrate and cantharides, showed that similar lesions occurred in the kidneys and choroid plexus. Poisons that affected the tubules of the kidney were apt to involve the epithelial cells of the choroid plexus. Similarly, there was a close parallelism between the alterations in the glomeruli

of the former and in the vascular system of the latter. An attempt was made to determine the effect of changes in the choroid plexus on the excretion of sodium iodide and lactose in the cerebrospinal fluid. Although the results obtained were not entirely satisfactory, it was found that animals treated with various poisons exhibited differences in the excretion of these substances. Lactose was also administered to several patients suffering from mental disorders, and the spinal fluid was examined at ten minute intervals for one hour and a half. In dementia paralytica and schizophrenia the amount of sugar in the spinal fluid showed little variation after this procedure, whereas in Parkinson's disease and senile dementia a rapid rise occurred. While the number of cases was small, the authors feel justified in stating that patients with different types of mental disease exhibit differences in the quantity of sugar that passes into the spinal fluid. Their experiments would seem to indicate that the formation of cerebrospinal fluid is governed by mechanisms that are analogous to those concerned in the production of urine. In their opinion, dialysis occurs through the vessels of the choroid plexus. The dialysate is then changed to a secretion by the action of the epithelial cells of the plexus. ROTHSCHILD, Foxborough, Mass. [Arch. Neurol. & Psychiat.]

ELECTRICAL STIMULATION OF THE BASAL GANGLIA IN A CASE OF ANENCEPHALY. ROY GRINKER, Ztschr. f. d. ges. Neurol. u. Psychiat. **135**:573, 1931.

Grinker had the opportunity to study an anencephalic monster which lived for four days; he stimulated the basal ganglion region electrically. The infant had a large spina bifida in the lumbar region. It cried and yawned, made sucking movements with tongue and lips and swallowed fluids. The eyes were in divergence and deviated downward; the pupils did not react to light. Auditory reflexes, Moro's reflex and tonic neck reflexes were not present. No spontaneous movements were made by the child except for a few purposeless motions. The child could move its head when placed on its stomach. The deep reflexes were active. The face was normally developed, but the eyes were very prominent. The cranial vault was open in the parieto-occipital region, and in place of the bony calvarium there was a soft, red-brown membrane, which was covered by a skinlike membrane. When this was opened, a slightly yellow fluid escaped. No brain tissue could be seen, but a pair of protuberances were found which appeared to be the corpora striata. These were stimulated by a weak faradic current with bipolar electrodes. Stimulation of the right side produced a slow flexion of the left elbow against the abdomen. The hip, too, was flexed. At the same time the knee was slightly bent, and athetoid movements appeared in the hands and fingers. The head and neck remained absolutely quiet. All the movements ceased with cessation of the current. When the left side was stimulated, similar movements appeared on the right. Repetition of the experiment produced the same result constantly. When the most oral part of the protuberances was stimulated, movements of the opposite arms and to a lesser degree of the legs were noted. Stimulation of the most caudal portion caused movements both of arms and of legs. Lateral stimulation caused no movements at all.

The child lived for two days after the experiments and behaved like a normal infant. It cried, slept and took nourishment from a dropper.

Microscopic study showed that the tissue mass on the surface was connective tissue. There was much inflammation in the specimen, and this interfered somewhat with the interpretation of the findings. In a few places sclerotic cortical tissue was found; it contained neither ganglion cells nor nerve fibers. Ependymal tissue was present in large quantities. The hypophysis and gasserian ganglion were identified. The spinal cord, medulla and periaqueductal region were normally developed. There were no axis-cylinders in the pyramids and pes pedunculi. The midbrain was normal. The portion that was stimulated was identified as the corpus striatum.

In higher mammals, stimulation of the corpus striatum has resulted in motor reactions only inconstantly. When positive effects have been obtained they have

been attributed to aberrant pyramidal fibers passing through the caudate nucleus. The pyramidal tracts were entirely lacking in this case, and the motor reactions, namely, athetoid movements and slow flexion, can be attributed safely to the basal ganglions, that is, the corpus striatum.

ALPERS, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

Diseases of the Ear, Nose and Throat

POSTTONSILLITIS GRAVITATION ABSCESSES. W. MEYER, Arch. f. Ohrenh-, Nasen- u. Kehlkopfh. **131**:125 (April 25) 1932.

Meyer reports a case of a circumscribed gravitation abscess originating in the peritonsillar region and descending into the mediastinum which healed without surgical intervention other than incision of the peritonsillar abscess from which the suppuration spread. In this case, eleven days after incision of a large peritonsillar abscess, occurring in connection with tonsillitis, the patient vomited a large amount of green pus. Roentgenologic visualization of the abscess cavity by injection of an opaque fluid showed that suppuration descended into the spatium retropharyngeum and the posterior portion of the mediastinum between the esophagus and the spinal column ending in the thorax at the level of the fourth thoracic vertebra. As esophagoscopy showed that there was a rather broad strip of apparently healthy mediastinal connective tissue between the abscess and the esophagus, drainage by division of the esophagus was not undertaken. With rest in bed and elevation of the pelvis the patient improved rapidly. Roentgenoscopy after six days showed a completely normal thorax; the lungs and mediastinum were clear, and no trace of the opaque mediums remained. Visualization with a contrast fluid may be recommended as a diagnostic aid. The achievement of complete cure by conservative therapy should lead to careful evaluation of surgical successes in similar cases. The necessity of differentiating between a circumscribed gravitation abscess and the much more frequent phlegmons in the throat with general septic symptoms is stressed. EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

SURGICAL THERAPY OF POSTTONSILLITIC SEPTICEMIA. G. HOFER, Monatschr. f. Ohrenh. **66**:587 (May) 1932.

Hofer thinks that surgical intervention in posttonsillitic septicemia should be undertaken in the earliest stage of propagation of the infection. In all cases in which this propagation is attended by chills, the first real chill should be considered an indication for intervention. The clinical manifestations of posttonsillitic septicemia are variable. Severe chill followed by collapse is the chief general symptom; it is an unequivocal sign of the spread of infectious matter into the blood stream. Locally, a severe tonsillitis is usually followed by the formation of abscesses which form the basis for a septic condition. The large venous trunks in the neck may be sensitive to pressure, especially in cases of extensive thrombosis, but the pressure sensitivity may be lacking as the disease may take its malignant course without extensive thrombosis of the large blood vessels, especially in the case of primary spread of infectious material into the blood stream. In cases with extensive suppuration of the cellular tissue of the neck, the pressure sensitivity is usually pronounced, and early intervention is clearly indicated. The author demonstrates by two case reports that good results can be achieved by ligation of the jugular vein and exclusion of the primary septic focus immediately after onset of the first clinical manifestation of tonsillogenous septicemia, even when no inflammation of the cervical tissue or the sheath of the vessel is demonstrable. In both cases the operation was undertaken within one-half hour of a chill (the first), which had followed soon after draining of an abscess. Collapse of the internal jugular vein in both cases permits the conclusion that there may have been a mycotic venous thrombosis higher up. The author considers location of, and intervention in, the mycotic thromboses not only difficult and dangerous but sometimes impossible. Exclusion of the primary

focus, whether still active or not, and interruption of the chief downward route of propagation, the jugular vein, is the first therapeutic requisite, but to be effective it must be undertaken in the first stage of the disease, after the first chill.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

EXPERIENCES WITH 1,600 TONSILLECTOMIES. ERDÉLYI, Monatschr. f. Ohrenh. **66**:596 (April-May) 1932.

Erdélyi discusses tonsillectomy on the basis of his experience with 1,600 cases; he dwells especially on precautions to be taken during tonsillectomy, complications, beneficial results and indications for intervention. The author experienced only 7 secondary hemorrhages among 1,600 tonsillectomies; he attributes this and the absence of other complications to strict adherence to the principles of general surgery, including very careful hemostasis. All blood vessels in adults are ligated before division, if possible, or otherwise immediately afterward. In children, if the operation is performed under ether rausch, all the vessels that are bleeding one to two minutes after tamponade are ligated. Large superficial veins at the base of the wound should be ligated at two points and severed to prevent spontaneous rupture and thrombosis later. The favorable results compensate for the five or ten minute increase in operation time. Waiting until the patient has fully recovered from tonsillitis or any complication of it and is in good general condition helps to prevent complications following tonsillectomy. The danger of abscesses of the lungs is decreased by performing the operation under local anesthesia. Very young or restless children may be operated on under ether rausch, which weakens, but does not destroy, reflexes, preventing aspiration of blood. The beneficial effect of tonsillectomy on the physical and mental development of children and their resistance to infectious diseases and on rheumatic diseases is stressed. As local indications for tonsillectomy, the author lists hypertrophy (usually in children), recurrent acute tonsillitis with high fever, recurrent peritonsillitis and chronic tonsillitis. Hypertrophy in the absence of pathologic changes is not an indication for tonsillectomy unless exact anamnesis furnishes support for the intervention or breathing and swallowing are interfered with. Chronic tonsillitis is an indication only if there are symptoms of recurrence or exacerbations or other concomitant conditions. Among diseases often originating in tonsillitis which may be considered indications for tonsillectomy he lists rheumatic polyarthritis, certain diseases of the cardiovascular system, acute and chronic nephritis and inflammation of the cervical lymph nodes. In tuberculosis, tonsillectomy may be performed only on absolute indication and in active cases only if life is endangered. EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TRACHEOBRONCHOSCOPY IN CHILDREN. F. HASLINGER, Monatschr. f. Ohrenh. **66**:621 (May) 1932.

Haslinger describes a tubular spatula which he has devised to simplify the introduction of the bronchoscope in children. The distal portion is not perfectly circular in cross-section, but is so shaped on one side that it fits into the angle at the point where the vocal cords are attached to the thyroid cartilage. With this spatula it is possible to view the anterior portion of the larynx, which is not possible with a flat or simple circular spatula. This spatula may also have a slightly larger diameter than a spherical or flat instrument. The spatula has a double approach, one through the axis of the tube through which the examiner looks and by which illumination is accomplished, and another, slightly to one side of this, through which the bronchoscope is introduced. It is so devised that the tongue cannot hinder the lateral approach. In endolaryngeal intervention surgical instruments can be introduced through the lateral opening.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

CLINICAL DIAGNOSIS OF INTRANASAL MENINGOCELE. O. HALLERMANN, Ztschr. f. Hals-, Nasen- u. Ohrenh. **30**:413 (May 13) 1932.

In connection with his personal experience with a case of intranasal meningocele in which exploratory puncture (just as in seven of the eight cases reported in the literature) produced fatal meningitis, Hallermann presents some diagnostic symptoms which he hopes will help clinicians to diagnose these cases without the dangerous intervention of puncture or biopsy. In cases of intranasal meningocele the hernia opening is in the region of the lamina cribrosa. The hernia protrudes through the opening in the ethmoid into the nose, pushing the mucous membrane of the roof of the olfactory fissure and the nasal septum before it, forcing the septum to the opposite side and pushing the ethmoid and median turbinate of the same side in a lateral direction. Rhinoscopy reveals a tumor-like downward protrusion covered with mucous membrane which more or less fills the interior of the nose; it is not pedunculate but rather continuous with the mucous membrane of the septum, at most permitting introduction of a probe between it and the lateral nasal wall. Another diagnostic characteristic of the tumor is its elasticity, tested by light pressure with a probe, and possibly pulsation. Increase of the brain pressure by compression of both jugular veins results in a loss of elasticity and increased hardness of the tumor. One or all of these characteristics should permit a meningocele to be differentiated from: polyps, which are usually movable and can be felt on all sides by a probe; fibromas, which are of tougher consistency, bleed easily at the touch of a probe and do not change consistency at increase of brain pressure, and finally malignant tumors, which usually have an uneven surface, are ulcerated and appear in persons of advanced age. Certain aspects of the facial portion of the skull may also give support to the diagnosis of meningocele: (1) widening of the root of the nose, (2) eyes unusually far apart and (3) other congenital disturbances, such as facial clefts or epicanthus. If the hernia is small and pedunculate it can be surgically exposed from the exterior and ligated, but in the majority of cases there is no pedicle and intervention is out of the question. EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

PATHOGENESIS OF TUBERCULOSIS OF THE MIDDLE EAR. G. THEISSING, Ztschr. f. Laryng., Rhin. (Teil 1: Folia oto-laryng.) **22**:328 (April) 1932.

After a general discussion of the question of the pathogenesis of tuberculosis of the middle ear, including a review of the literature, Theissing reports his own investigations on this subject. Examinations of twenty-nine temporal bones of nineteen children and young adults who died of generalized tuberculosis gave evidence of the hematogenous origin of the tuberculosis of the middle ear which was found to exist in all but one of the cases. Tuberculous foci in the bone marrow occurred almost regularly, especially in children. In the majority of cases the bone marrow was the only seat of tuberculosis of the middle ear. One of the chief arguments against a hematogenous development of this disease, that an isolated tuberculosis of the bone of the mastoid process had never been observed, was thereby nullified. Four cases in which tuberculous changes of the bone marrow existed without the slightest manifestation of any disease of the mucous membrane of the middle ear are especially significant. Brieger's argument against the hematogenous route of infection, that the middle ear is not often affected in general miliary tuberculosis is refuted by the findings in these cases, most of which showed a more or less extensive miliary dissemination. The assumption of the hematogenous origin of tuberculosis of the middle ear based on these observations was given further support by animal experiments. The author produced tuberculous infection of the middle ear and bone marrow of the temporal bone in rabbits and guinea-pigs by injection of virulent tubercle bacilli into the common carotid artery. The use of coarse emulsions of cultures of tubercle bacilli is essential for producing infection by this method. Hitherto the only experimental method of producing tuberculous infection of the middle ear was by direct infection of the tympanic membrane which is rare in the spontaneous develop-

ment of the disease; the author's method uses the route that is of most importance from the modern point of view. The tuberculous changes in the ears of the animals so infected were similar to those in the human cases reported. The tuberculous manifestations usually appeared in the mucous membrane and the bone marrow at the same time and equally, or sometimes in the latter alone, rather than starting in the upper layers of the mucous membrane and gradually extending downward to the bone as in previous experiments. The experiments, besides supporting the assumption of the otogenous origin of tuberculosis of the middle ear, prove that the notion that the primary localization of tuberculosis of the ear is exclusively in the mucous membrane is no longer tenable.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

A CASE OF HEALED SUBACUTE OTITIS WITH SECONDARY LOCALIZED CEREBRAL SYMPTOMS. V. HLAVAČEK, Časop. lék. česk. **69**:1041 (July 11) 1930.

A boy aged 9 years, who had had scarlet fever and otitis media three years previously, which had lasted only several weeks, came to the hospital with a purulent otitis of three weeks' duration. There was an indurated, red painful, but not fluctuating mass over the zygoma. The temperature was septic; the aural canal discharged thin, yellow pus, and the mastoid was tender. Antrotomy was performed with the patient under general anesthesia. A week later vomiting was followed by an evanescent urticarial rash and a slow response to questions. Two days later, epileptiform clonicotonic convulsions, facial palsy and coma appeared. Both the upper and the lower extremities were involved. There was a loss of abdominal, cremasteric and tendinous reflexes. Another operation revealed an inflammatory reaction about the root of the zygoma and a purulent membrane. The dura was tense. Puncture revealed clear fluid. Complete paralysis of the contralateral upper and lower extremities was followed by a slow recovery. Symptoms of this type may take place with increased intracranial pressure due to an extradural pathologic process, but they are not followed by paralysis and are only of short duration. The symptoms point to involvement of the hemisphere motor centers. A review of the literature is given, in which Körner's series are cited. Two cases occurring in the age group of from 4 to 7 years, eight cases in that from 10 to 15, four cases in that from 20 to 25, four cases in that from 30 to 38, and one case in a person 51 years of age are reported.

STULIK, Chicago.

Diseases of the Skin

JUVENILE ACRODYNIA: REPORT OF ELEVEN CASES. STANLEY CRAWFORD, Arch. Dermat. & Syph. **26**:215 (Aug.) 1932.

The author thoroughly reviews the history of acrodynia. He discusses the three theories of causation, infection, avitaminosis and dysfunction of the vegetative nervous system. The symptomatology, prognosis and treatment are also discussed, with special emphasis given to the value of dietary measures in the management of the disease. A detailed report of eleven cases is included.

EKERMEYER, Iowa City.

DERMATITIS VENENATA: REPORT OF A CASE DUE TO THE OSAGE ORANGE. ALBERT SCHUR, Arch. Dermat. & Syph. **26**:312 (Aug.) 1932.

This is a report of rare dermatitis venenata caused by contact with the Osage orange. The fruit is found in the middle-western and eastern portions of the United States. The bark is used in dye-making and the trunk in tanning leather.

The author believes that the disease occurs more frequently than is supposed, and is probably often overlooked and reported as a plant or industrial dermatosis of undetermined origin.

EKERMEYER, Iowa City.

METABOLIC STUDIES IN URTICARIA: 1. ACID-BASE BALANCE. 2. BLOOD CHEMISTRY. LEO H. CRIEP, J. Allergy **3**:219 (March) 1932.

The carbon dioxide-combining power and the content in the blood of calcium, chlorides, urea, uric acid, creatinine and nonprotein nitrogen were studied. Forty urticarial patients between the ages of 11 and 65 years were used. All of the investigations were not made on all of the patients; however, the only variance from normal was in the uric acid content, which was slightly increased, and in the chlorides, which were slightly decreased during the attack.

HOYER, Cincinnati.

THE ETIOLOGY OF ERYTHROEDEMA. W. J. PENFOLD, HILDRED M. BUTLER and I. JEFFREYS WOOD, M. J. Australia **2**:127 (July 30) 1932.

Cultures of the blood were made in fifteen cases, specimens of the blood being taken at various stages of the disease. On Kendall's K. medium, positive results were obtained in three cases. The other attempts gave negative results. The organisms obtained were gram-positive coccoid forms of variable size and shape. The evidence is insufficient to indicate whether the organisms are etiologically related to the disease, but the organisms found were so peculiar as to merit further examination.

RATTNER, Chicago. [ARCH. DERMAT. & SYPH.]

UNDESIRED PERMANENT ALOPECIA FOLLOWING ROENTGEN RADIATION: EXCUSABLE ROENTGEN ACCIDENTS. KARL HOEDE, Dermat. Wchnschr. **94**:410 (March 19) 1932.

The author reviews the opinions of various authorities in regard to the dosage and possibility of accidents in roentgen epilation for ringworm. He reports a single case of permanent alopecia in a series of 137 children. It occurred in one of two brothers irradiated on the same day (in 1921). He concludes that an untraceable error in technic occurred. The epilation dose should not exceed 80 per cent of a skin erythema dose for adults or 50, 60 or 70 per cent for children, according to age.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

TEMPORARY AND PERMANENT ALOPECIA FOLLOWING ROENTGEN RADIATION. W. MEMORSKI, Dermat. Wchnschr. **94**:513 (April 9) 1932.

The author reports the occurrence of temporary alopecia in two adults following roentgen examinations of the sinuses. In a third case, a girl, aged 3 years, had total alopecia. There was no evidence of dystrophy of the internal glands or of a hereditary taint. The author concludes that the alopecia was due to the roentgen examination made of the renal region of the mother in the sixth month of her pregnancy.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

THE LOSS OF HAIR IN THALLIUM POISONING. V. KOSZLER, Wien. Arch. f. inn. Med. **22**:473 (July 15) 1932.

The author describes a case of thallium poisoning which had a favorable outcome in spite of the ingestion of a large dose.

Atypical symptoms noted were paralysis of the phrenic and the recurrent nerves and trophic disturbances of the skin, nails and hair. A connection between the loss of hair and abnormality in the vegetative endocrine system could not be definitely established.

SCHLUTZ, Chicago.

Surgery and Orthopedics

A STUDY OF MESENTERIC CYSTS. J. OGLE WARFIELD, JR., Ann. Surg. **96**:329 (Sept.) 1932.

To date approximately five hundred cases of mesenteric cyst have been reported. One half of these tumors occur in the small intestine and one fourth of them in

the mesentery of the ileum. There are no pathognomonic signs or symptoms. The tumors may be so small that they cannot be palpated or so large that they practically fill the entire abdomen. The greater majority are single cysts, although a few multiple tumors have been recorded.

The most frequent and serious complication of mesenteric cysts is intestinal obstruction. It occurs in one third of the cases, and in these the mortality is 50 per cent. Other complications are peritonitis, a sequel to obstruction, hemorrhage into the cyst, rupture of the cyst, torsion of the cyst or impaction of the cyst in the pelvis.

The treatment is surgical. In acute cases, the treatment is directed principally toward the complications, the chief of which is intestinal obstruction, while in the subacute and chronic cases the operation consists in removing or obliterating the mesenteric cyst by one of the following methods: (1) enucleation (2) enucleation with intestinal resection or (3) drainage or marsupialization.

BANTIN, Omaha.

MESENTERIC AND OMENTAL CYSTS. EDWARD W. PETERSON, Ann. Surg. **96**:340 (Sept.) 1932.

The author reports in detail five cases of mesenteric cyst and one of omental cyst in which the patients were operated on without mortality. In each case the symptoms presented were somewhat different, simulating such conditions as appendicitis, indefinite abdominal pains and intestinal obstruction.

The treatment recommended and used in each case was surgical, either enucleation, resection or drainage being used.

In concluding, the author aptly states that: "If all the cases met with in practice could be put on record, the condition would no longer be considered rare.

"Unless teachers of surgery make occasional mention of and unless future works on surgery place more emphasis upon this topic, failures to make correct preoperative diagnosis will continue to be the rule and surgical mortality and morbidity will remain unnecessarily high."

BANTIN, Omaha.

EMPYEMA NECESSITATIS. A. MATHESON and MAURICE S. MAZEL, Arch. Pediat. **49**:330 (May) 1932.

The author reports a case of empyema necessitatis.

WADDELL, University, Va.

RANULA: REPORT OF A CASE. J. ORTON GOODSELL, Dental Cosmos **74**:968 (Oct.) 1932.

The author describes a case of ranula occurring in a boy 7 years of age. The term ranula usually applies to swellings or cysts in the floor of the mouth underneath the tongue, resulting from obstructions in the excretory ducts of the glands. The record for the preoperative period showed that the swelling was first noticed a short time after birth, at which time it was opened. When the patient was about 1 year of age, the swelling was again present; at that time it was aspirated, with the extraction of fluid.

The swelling again made its appearance and increased in size to the extent that it filled the mouth, causing atrophy of the musculature of the tongue, malocclusion of the teeth, faulty speech and a constant flow of saliva from the corners of the mouth. Such was the picture when the patient was first seen by the author.

The author's treatment consisted in complete enucleation of the cyst. Several months later all symptoms disappeared; muscular exercises for the tongue resulted in good speech.

MARKUS, Philadelphia.

ORTHOPEDIC TREATMENT OF ANTERIOR POLIOMYELITIS. HERBERT C. FETT, New York State J. Med. **32**:859 (July 15) 1932.

Orthopedic care should be started as soon as possible after the disease is recognized. The value of immobilization and of hydrotherapy is stressed. Massage, muscle reeducation and rest are necessary.

AIKMAN, Rochester, New York.

DIAGNOSIS OF ABDOMINAL CYSTS WITH THE AID OF PNEUMOPERITONEUM. R. BOLLER and R. PAPE, Wien. Arch. f. inn. Med. **22**:161 (April) 1932.

The authors report two cases in which the procedure of producing a pneumoperitoneum enabled them to discover tumors in the abdomen which proved to be cysts. The procedure should never be undertaken if meteorism is a pronounced symptom or if chronic ileus is present. The maximum of air that can be introduced intraperitoneally is between 800 and 1,200 cc. The procedure is valuable in differentiating between ascites and cystic tumors. In some cases it will enable one to detect fluid in the abdomen.

SCHLUTZ, Chicago.

RECOGNITION AND TREATMENT OF SO-CALLED CONGENITAL LUXATION OF THE HIP IN THE INFANT. H. TIMMER, Nederl. tijdschr. v. geneesk. **76**:1202 (March 12) 1932.

For a good prognosis, it is desirable that congenital luxation of the hip is treated during infancy, in every case before the end of the third year of life. Some indications for a good prognosis and early clinical diagnosis are given, as well as a survey of the roentgenologic findings and of modern treatment.

VAN CREVELD, Amsterdam, Holland.

Miscellaneous

PREVENTIVE MEDICINE AS RELATED TO PEDIATRICS. JOE T. SMITH, Arch. Pediat. **49**:639 (Oct.) 1932.

The writer reviews the present knowledge of proved preventive measures. The subject is approached from the standpoint of infant feeding and hygiene, periodic health examinations, public health procedures and specific preventive methods.

WADDELL, University, Va.

DENTAL AGENESIS IN THE PRESENCE OF DIABETES MELLITUS. GEORGE A. HECTOR and DONALD G. EVANS, Dental Cosmos **74**:990 (Oct.) 1932.

The author reports a case of diabetes mellitus in a girl, aged 11 years. The family history shows that diabetes mellitus, tuberculosis and defective formation of the teeth occurred on the maternal and the paternal sides through several generations. Physical examination revealed an undernourished child.

The dental picture showed that the teeth had little or no crowns and extended just above the level of the gums. The formation of enamel was defective. The roots were all well formed, and the cortical and epiphyseal areas of the long bones were well calcified.

The author does not feel that any single disease is responsible for the agenesis, although the appearance of this condition in the members of the family is too constant for coincidence.

MARKUS, Philadelphia.

A TYPE OF DRUG ALLERGY CAUSED BY CONTACT SENSITIVENESS TO ETHER AND TO CHLORINE. W. W. DUKE, J. Allergy **3**:495 (July) 1932.

A boy was sensitive to ether, asthma, cough and coryza being caused when it was inhaled. A drop of ether on the skin produced a wheal with pseudopods at the site of contact. Passive transfer could not be conferred to normal skin.

A physician was sensitive to the fumes of chlorine which escaped from solution of chlorinated soda. Inhalation of the fumes would cause a cough, coryza and asthma. Chlorine water applied to the skin produced a wheal with pseudopods at the site of exposure. Passive transfer could not be transferred to the normal skin. Relief could be obtained by the inhalation of aromatic spirits of ammonia, which formed ammonium chloride.

HOYER, Cincinnati.

AMERICAN ACADEMY OF PEDIATRICS: PROGRAM FOR STATE COMMITTEE. HAROLD C. STUART, New England J. Med. **207**:114 (July 21) 1932.

There are many reasons for believing that the personal physician is in the most strategic position for supervising the health of normal children. Other things being equal, he is the one best fitted to determine what a person's health needs are, and how they may best be met. Thorough and systematic health supervisory service is not generally offered by the physicians of the state to the children whom they consider members of their clientele.

The State Committee of the American Academy of Pediatrics realizes that the provision of better health service for children is one of the primary objectives of the society.

Preventive pediatric supervision of normal children is a fundamental part of pediatric practice. Therefore, improvement in the amount and quality of such service is an objective of the Academy. Through its general extension and improvement, there is great promise of further reduction of morbidity and mortality and of better protection of normal growth.

The academy accepts the following objectives of the White House Conference as expressed in the Children's Charter:

"For *every child* full preparation for his birth, his mother receiving prenatal, natal, and postnatal care; . . . .

"For *every child* health protection from birth through adolescence, including periodic health examinations. . . ."

The State Committee hopes to be of assistance to physicians in the following ways: (1) in the preparation of literature that will cover briefly and practically the subjects dealt with in health service; (2) in the provision of opportunities for physicians to visit health conferences in Boston, or elsewhere in the state, and the observation of the kind of service that is rendered, and (3) in the bringing of these subjects to the attention of local medical societies.

GENGENBACH, Denver.

THE POINT OF VIEW OF CHILDREN'S HOSPITAL AND PEDIATRICIAN. HAROLD C. STUART, New England J. Med. **207**:140 (July 21) 1932.

From the literature of from ten to twenty years ago dealing with gonorrheal vulvovaginitis in children, it is apparent that an almost hysterical dread of the disease developed among those responsible for the institutional care of children. For example, Hess reported that 50 per cent of the girls applying for admission to the New York Foundling Society had to be turned away because of the finding of this disease.

The author presents a few figures based upon observations made at the Infants' Hospital and the Children's Hospital, Boston. The Infants' Hospital has admitted about 15,500 infants under 2 years of age since 1915. During that time the diagnosis of gonorrheal vulvovaginitis has been made twelve times and of nongonorrheal vaginitis five times. No case with a positive smear for gonorrhea has been encountered in the past twelve years. In spite of the fact that vaginal smears have not been required as a routine on admission for the past six or seven years, not only has there been no epidemic spread within the hospital, but there has not been a single recorded case traceable to infection in the hospital.

The Children's Hospital of Boston has received in its wards or outpatient department about 16,000 children annually in the five year period from 1926 to 1930. The diagnosis of vulvovaginitis was made on the average of about fifty times a year, and a review of these cases suggests that not more than twenty per year were of positive gonorrheal infections. In a special gynecologic clinic conducted at the hospital to treat patients with positive or suspicious cases, Dr. Hudson in 1927 found only nine positive reactions in twenty-seven patients referred; and in 1929, seven positive reactions in forty-one referred. The smears taken in this special clinic were cervical in origin, as a careful instrumental inspection for diagnostic purposes was a routine measure.

The Children's Hospital in 1930 discontinued its gynecologic clinic because of inadequate demand for its service.

The pathologic department at the Children's Hospital, during the past year and a half, has been taking routine sections of the cervix and vagina of girls coming to postmortem examination. Not one of the fifty cases reviewed by Dr. Farber showed gonococci or even a suspicious organism in the section.

In the birth registration area of the United States the diagnosis of gonococcus infection (all forms) was made sixty-four times in girls under 10 years of age in 1914, and forty-seven times in 1928. Correcting for the increase in the size of the area in this interval, there has been more than 50 per cent reduction in the incidence of death during this time.

The pediatrician of today, on the basis of experiences similar to those presented, is convinced that gonorrheal vaginitis is not, in its usual form and under reasonable conditions of hygiene, so acutely communicable as was previously thought, and that there has been a marked reduction in its incidence in recent years.

GENGENBACH, Denver.

INGESTION OF LIVE INSECTS BY AN INFANT. F. BACCHERONI, Prat. pediat. **10:** 271 (June) 1932.

After a baffling illness of three days' duration, characterized by vomiting and convulsions, an 8 month old baby finally vomited a dozen partially digested cockroaches, and was relieved completely.

DOOLEY, Kent, Conn.

FATAL, MEDICINAL POISONING WITH CHENOPODIUM OIL. G. SCHRADER, Samml. v. Vergiftungsfällen **3:**79, 1932.

A 4½ year old child was given a capsule containing 16 drops of chenopodium oil as a vermifuge, and two days later was given 32 drops, since the first dose had been ineffective. Death occurred in about twenty-two hours, after a period of illness characterized by convulsions, cyanosis and coma. At necropsy, the small bowel was markedly inflamed; the solitary lymph nodes and Peyer's patches were hyperemic, as were also the mesenteric lymph nodes, the brain and the meninges. Status thymicolymphaticus was a contributory factor. Chenopodium oil was recovered from various organs. In this instance the maximum adult dose of 0.5 Gm. had been exceeded in a child.

RUKSTINAT, Chicago. [ARCH. PATH.]

Society Transactions

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

JOHN P. PARSONS, M.D., *Secretary*

Ann Arbor, Mich., Nov. 11 and 12, 1932

HENRY G. PONCHER, M.D., *President*

NUTRITIONAL ANEMIA IN INFANCY. DR. HENRY G. PONCHER.

Nutritional anemia in infancy is not a chronological division of this symptom for a certain age period. It is a dynamic conception based on the recognition of a difference in metabolism, growth and anatomy. The hemoglobin level during infancy varies clinically with circumstances that affect these factors. Thus, normal premature infants, twins and rapidly growing infants have a lower hemoglobin level than normal full-term infants, if no provision is made for their difference in requirements. While nutritional anemia is directly on a dietetic basis, such predisposing factors as rapid rate of growth, hemorrhage and infection are important factors at this period of life. Thus, in the majority of cases it is the increased demand that is placed on the infant chiefly by rapid growth, hemorrhage and infection that results in nutritional anemia rather than a deficiency in iron due to a low intake.

DISCUSSION

DR. EDWARDS: Do you believe that rate of growth is a factor in anemia? Would you curtail the growth of children who grow too rapidly?

DR. HENRY G. PONCHER: I believe that special consideration should be given to rapidly growing infants. Iron-containing foods should be added to the diet at an earlier period in such cases. Growth is not a continuous process, however, and it is a common experience to find that in a normal full-term infant a hemoglobin level which is below normal at one period rises to normal at a later date with no change in diet or in treatment. It is for this reason that I believe it is well to look on nutritional anemia from the physiologic point of view rather than to regard it as a morbid entity that responds to iron, copper or liver therapy.

DR. D. MURRAY COWIE: In cases of nutritional anemia large doses of beef juice should be given in addition to large doses of iron. The juice of a pound of round steak a day, I am sure, causes the hemoglobin to rise much more quickly and effectively than if it is omitted and iron alone is used. The beef juice probably acts by stimulating nutrition. It has been taught that iron acts in the same way.

EXPERIMENTAL STUDIES IN IRON METABOLISM. DR. HERMAN H. RIECKER.

The behavior of iron is similar to that of lead calcium and phosphorus in that its retention and excretion are controlled by the p_H of the body. This has been shown in experiments on normal subjects, patients and a dog, a diet neutral as to its salts being used and sodium bicarbonate or ammonium chloride added to change the p_H of the body fluids.

The addition of sodium bicarbonate to the neutral diet causes a marked increase in the output of iron in both urine and stool. A normal dog was made anemic by this method when it was carried out over a long period with the dog on the normal maintenance intake of iron. In eleven days an excess excretion of 30 mg. over the intake was secured.

In a patient with pernicious anemia who was under treatment the excretion of iron in the urine alone was doubled by the addition of 8 Gm. of sodium bicarbonate daily to the neutral diet. Retention of iron by the addition of an acid salt (ammonium chloride) was not obtained unless decreased renal function enabled mild acidosis to occur.

The highly alkaline diet low in iron has been used favorably for treatment in a case of polycythemia vera.

The principle involved in these experiments has not been applied to nutritional anemia in children, although possibly it would play some part in the mechanism of such anemias.

DISCUSSION

DR. D. MURRAY COWIE: What happens in the case of peptic ulcer with or without hemorrhage when one uses the so-called Sippy treatment with large amounts of sodium bicarbonate? The results of your observations might furnish a contraindication to this method of treatment. I have frequently used large doses of sodium bicarbonate for hyperchlorhydria over long periods of time, in fact, months, without stopping. Of course it is known that in cases of hemorrhage the hemoglobin finally returns to normal while the carbonate is being administered. I am wondering if it would respond more quickly should the carbonate be omitted. As a matter of fact, carbonate is not necessary. I have not noted any change in the hemoglobin, but it may be that this point has not been watched as carefully as it should be. I imagine many of these patients have been on a neutral diet. The usual diet for ulcer, I believe, will figure out that way.

DR. JOHN P. PARSONS: There is no question but that any particular salt that must be absorbed must be in some available form; that is, it must be soluble. But the mere fact that it is soluble does not mean that it will be absorbed. This is a common observation in general physiology, especially in plant physiology. It is not uncommon to see a plant starve in a soil that contains all the food constituents that are necessary. If the reaction of the soil is changed so that it becomes alkaline by the addition of ash or by changing it to an acid reaction, rapid absorption may occur. The horticulturist goes still further and picks out a particular salt in the way of a fertilizer. In other words, the absorbing tissue may be normal, the constituents to be absorbed may be soluble, and yet the process fails because some particular thing is lacking, a specific enzyme or a salt. In other words, some specific thing is lacking that is classified as a catalyzer.

DR. HERMAN H. RIECKER: Several cases of ulcer have come to my attention in which anemia developed apparently owing to the alkalosis of a Sippy regimen, and cleared up without iron when the medication was discontinued. Incidentally, the rationale of large doses of iron is based on its comparative insolubility in the small intestine where a large surface must be contacted to insure absorption. This observation was made by A. B. Macallum in 1895.

TREATMENT OF DIPHTHERIA IN CERTAIN CLINICS ABROAD. DR. MARK F. OSTERLIN.

While studying in Germany during 1931-1932, I spent three months at the Kinderkrankenhaus in Berlin. I was interested to observe that diphtheria is not treated as requiring emergency measures unless intubation or tracheotomy is necessary. Patients entering a clinic during the late afternoon or night are often not seen until the next morning when the rounds of the ward are made, at which time the dosage of serum is prescribed. The patient receives the serum after the rounds are completed.

The dosage of serum is rather small as compared with that used in the pediatric clinic of the University Hospital. In mild cases 300 units per kilogram of body weight and in toxic cases 500 units per kilogram are the usual amounts given, the average being from 10,000 to 20,000 units. Reactions from the serum are infrequent and mild.

Some clinicians expressed doubt as to the specificity of diphtheria antitoxin. They believe that normal horse serum will produce the same result. It is believed

that diphtheria is on the increase, and that more toxic cases are being seen. This is theoretically explained on the ground that the antitoxin may be changing the organism or that the organism is becoming resistant to the antitoxin. Immunization with toxin-antitoxin has not seemed to reduce the incidence of the disease. In Berlin, it is reported that approximately 600,000 children were given toxin-antitoxin; diphtheria developed in 5.8 per cent of those thus immunized, and in 6.2 per cent of those not immunized. No Schick tests were done. The number of toxic cases in both groups was the same. The difference of 0.4 per cent is of no consequence.

CIRCUMCISION IN GIRLS—WHEN AND WHY IT SHOULD BE PERFORMED; AN OPERATIVE PROCEDURE. DR. D. MURRAY COWIE.

The need for circumcision in girls is not of frequent occurrence. Sometimes it is necessary in order to overcome irritation, particularly when there is a marked discharge, which is not infrequently diagnosed as of vaginal origin, either specific or nonspecific. Bed wetting, pseudomasturbation and well known reflex disturbances may be influenced by the happenings that suggest the advisability of circumcision. Usually, however, adhesions and irritations can be overcome by careful manipulations and genital hygiene. Circumcisions in girls have not been generally successful. Adhesions reform, and the situation may be worse than before operation. A uniformly successful operative procedure is described and amply illustrated. A few case reports are added. Routine circumcision in girls should be condemned. A real need should be demonstrated before the operation is performed. Even though the clitoris in an infant is completely embedded, the developmental tendency is for it to emerge in due time.

COMPARATIVE STUDIES IN EXCRETION OF WATER AND SOLIDS BY ABNORMAL KIDNEYS. DR. FLOYD H. LASHMET.

Three groups of persons were studied made up of: (*a*) normal persons, (*b*) nephritic patients without edema and (*c*) nephritic patients with edema. Under conditions of extreme restriction of water, nephritic patients without edema excreted the normal amount of waste products, but in an abnormally large volume of urine. The extra water to make up the large volume of urine was obtained at the expense of water in the body. Under the same conditions, nephritic patients with edema excreted a small volume of urine and an abnormally small amount of waste products.

When water was allowed, the volume of urine increased in both groups, and also the normal amount of waste products was excreted.

Apparently, the mechanism of excretion of wastes in renal disease is one which avoids retention of these by excretion of a large volume of urine as a compensation for a low concentrating ability. If the intake of water is inadequate, water will be drawn from the body in order to make the necessary large volume of urine. If water cannot be released from the tissues, as in nephrotic patients with edema, then retention of waste products results. Regardless of whether edema is present or absent, a large intake of fluids is imperative if the kidneys are to do their work satisfactorily.

DISCUSSION

DR. JOHN P. PARSONS: This paper answers quite satisfactorily the original question I asked Dr. Lashmet several years ago, namely, phylogenically is the organism conditioned to save water or save solids? Dr. Lashmet's paper shows that the organism tries to save water; that is, it excretes the maximum amount of solids with the minimum amount of water.

DR. DANIEL BUDSON: When is the limit of water needed reached?

DR. FLOYD H. LASHMET: One of the most imperative questions is, in what way do the normal and the diseased kidneys differ in excretion of water and of solids. In what way do kidneys that are normal and abnormal differ in the excretion of water and of solids. It is known that under definite controlled con-

ditions people with normal kidneys can excrete a concentrated urine. Under the same conditions, people with renal disease are unable to make a urine with a specific gravity of 1.029. Suppose a person excreted a normal volume of urine but retained wastes. That patient would have a low specific gravity. Suppose a patient excreted a normal amount of waste products, but these waste products were contained in a large amount of urine. This patient would also have a low specific gravity. A small amount of solids in a large volume of urine indicates (1) retention and (2) dehydration. A small amount of total waste products in a large volume of urine indicates both dehydration and retention, which conditions exist in renal disease. If the kidneys attempt to eliminate waste products in a small amount of urine, they have to work to a maximal limit. Persons with renal disease cannot make a concentrated urine, and since they cannot, they must excrete a large amount of water in order to excrete a large amount of waste. If the intake of water is not sufficient to meet the requirement, the amount required will be obtained at the expense of the water in the body. This water is not available in the patient with nephrotic edema. The only hope the diseased kidneys have of getting rid of waste matter is by a regimen of forced fluids.

EXPERIMENTAL STUDIES ON LYSOZYM. DR. KAMEYO SADAKATA.

Stools from healthy breast-fed and artificially fed infants showed about equal numbers of gram-positive and gram-negative organisms. Stools from sick infants with gastro-intestinal manifestations showed more gram-negative organisms, some of them being loaded with colon bacilli. During the first month of the breast-fed babies had in their stools few gram-positive organisms, no sarcinae and none of the so-called lysodeiktic micrococci. These babies, however, received a small supplemental feeding of lactic acid milk. Meconium showed no bacteria in smear or in culture. Mucoid stools quite regularly showed large numbers of gram-negative bacilli.

Following the technic of Rosenthal and Lieberman, I estimated the lysozym action of various substances against standard suspensions of yellow sarcinae and colon bacilli. Confirming the work of others, lysozym was demonstrated in varying amounts in egg-white, meconium, stools from breast-fed babies and nasal secretions.

The lytic action of egg-white is greatly affected by the p_H. Undiluted egg-white has a p_H around 8.6. Its lytic power is slight as compared with solutions of 1:10 with p_H from 7.2 to 7.6. Variations in the p_H to either side of the last figures depress the lytic power of egg-white. Protein-free lysozym solutions may be prepared from egg-white.

Lysozym is present in mother's milk from the meconium period on. It is also present in milk taken directly from the cow's and the goat's udder. It is not present in commercial cow's milk or commercial goat's milk (p_H 6.8). Woman's milk contains the most lysozym, and cow's milk the next largest amount. Its action is preserved in cow's milk and goat's milk collected under sterile precautions and placed in the icebox for two weeks.

The stools from breast-fed babies regularly show lysozym action, as do also those from breast-fed babies given supplemental feedings of lactic acid milk. The stools from babies fed on pasteurized cow's or goat's milk do not contain lysozym. Because of the susceptibility of lysozym to changes in p_H, these observations indicate that the lysozym is inactivated by the gastric juice and reactivated by the intestinal secretions.

The secretions from the nose contain a lytic principle, which is active against standard suspensions of yellow sarcinae and colon bacilli. The action is slow but progressive; thus the colon bacillus is not killed or completely inactivated for forty-eight hours. There is suggestive evidence from my observations that the nasal "lysozym" may be stimulated to flow by the instillation of small amounts of physiologic solution of sodium chloride into the nasal passages, and that serous rhinitis may be improved by the use of purified lysozym in the form of nasal drops in infections of the upper respiratory tract.

DISCUSSION

DR. D. MURRAY COWIE: I assigned this research problem to Dr. Sadakata and have been much interested in checking her observations. Considerable investigation will have to be done before any conclusion can be arrived at as to the rôle of lysozym in infant feeding. If it is finally proved to be of value, instead of offering an argument in favor of the use of unpasteurized certified milk, it will suggest the advisability of adding lysozym after sterilization has been completed. Dr. Sadakata calls attention to the fact that commercial milk has a p_H below 6, a point that inhibits the action of lysozym. She also points out that the p_H of the stomach is high enough to inactivate lysozym, and that its presence in stools indicates that it is reactivated in the intestine. The same may happen with unheated milk. I believe direct observations on this point have not been concluded. Dr. Sadakata's work is part of a research problem being carried on by the University of Michigan Mead Johnson Research Fund.

HODGKIN'S DISEASE IN CHILDHOOD. DR. CLEMENT A. SMITH.

In the past six years there have been 22 cases of Hodgkin's disease in the pediatric clinic of the University Hospital. This number forms about one sixth of the total group of 132 cases of Hodgkin's disease in patients of all ages seen in the hospital during this period. In 18 of the 22 cases it was possible to follow the course. Thirteen have been fatal. None of the remaining 5 children are clinically well.

The age at onset varied from 18 months to 12½ years. The average age was slightly over 7 years. There were 20 boys and 2 girls. The cervical region was involved first in all but 2 cases, and the left cervical region alone was involved more often than the right. There were no characteristic presenting symptoms, the presence of the mass alone usually bringing the patient to the hospital. The average course of the disease before these patients were seen was about one year.

As the disease progressed, usually all the lymph tissue of the body became involved. The mediastinal glands and the spleen were each clinically involved in 10 cases, and the liver in 8. Fever of the Pel-Ebstein type occurred in 3 patients, all of whom died. In 2 of these the fever directly preceded death. Five other patients showed a marked daily swing in temperature. All of these died.

The average survival in the 13 fatal cases was two years and eleven months. That in the 5 cases in which the children are still living is three years and seven months. The length of life did not vary greatly with regard to the age of the patient at onset. Treatment was mainly by roentgen irradiation, but this therapy cannot be correctly evaluated chiefly because of lack of parental cooperation. The disease had an unusually rapid course, the period of survival from the date of onset averaging only seven months. Comparison of the cases in which roentgenotherapy was not used with the cases in which it was used is valueless. It is believed, however, that roentgenotherapy is the most effective way of producing a decrease in the granulomatous tissue. The method of early and frequent courses of intensive treatment is advocated. Leukopenia, unless the count is below 1,500, is not a contraindication to treatment, though, of course, the blood changes must be studied.

There was nothing specific about the blood in the 22 cases. The white count usually was within normal limits of variation. A moderate increase of the monocytes was common, as was the development of a profound primary type of anemia, the latter occurring as a rule only in terminal stages.

Biopsies or autopsies were performed in 21 of the 22 cases. Typical Hodgkin's disease was diagnosed in 18, but in 4 of these later examination showed progression to a sarcomatous form. Sarcomatous Hodgkin's disease was found originally in 3 other cases.

In 1 case the process—sarcomatous in type—seemed to originate in the cranial bones. The disease had a rapid course, and at autopsy all the lymphoid tissue as well as these bones was found involved. Another case, in which during four

years a typical Hodgkin's disease became sarcomatous, is interesting in that clinical pulmonary tuberculosis developed. For four more years this patient lived with coexisting tuberculosis and Hodgkin's disease, and died of tuberculous meningitis. Both conditions were found at autopsy.

Only eleven of the cases showed what might be interpreted as foci of infection. In 19, tuberculin tests were done, a negative reaction being obtained in 16. In 1 case in which the patient gave no history of tuberculous contact, there was a positive test, and in 2, including the case of clinical tuberculosis previously mentioned, there were indefinite reactions. The family history was unimportant in 21 cases. In 1 case there was a history of the death of a 9 year old brother from apparently proved Hodgkin's disease.

UNDULANT FEVER (BRUCELLA INFECTION) IN CHILDREN (PRELIMINARY REPORT). DR. JOHN F. SANDER, Lansing, Mich.

A short review of the literature on undulant fever was given in which the scarcity of reports on cases in children was noted. The observation was made that this disease is more common in children than is suspected, and that with improved methods of diagnosis and of treatment it will be more promptly recognized and treated in many children so afflicted.

These improved methods of diagnosis were given as an intradermal test with pure nucleoprotein prepared from cells of the organism, and if the result of the skin test is positive, determination of the absence of Brucella opsonins in the blood in a phagocytic system with citrated whole blood. The patients were treated with an agent called brucellin, developed at the Central Brucella Station at the Michigan State College, Lansing. (Complete reports of the use of the nucleoprotein intradermal test and the agent called brucellin will be reported on in a forthcoming paper by Dr. I. F. Huddleson of Michigan State College.)

Six cases were reported in which the condition had been diagnosed undulant fever and treatment given during the preceding six months. The patients ranged in age from 17 months to 11 years. They were all from the higher type of American home and had had well supervised diets. However, in each case there was a history of considerable quantities of raw milk having been consumed at some recent period before the onset of symptoms or of raw eggs having been used in the form of eggnogs at frequent intervals. The symptomatology varied not at all from that described in adults, and the differential diagnosis was pointed out as being difficult, because of the many diseases of a subacute and a chronic nature to which children are heir. Each child whose condition was diagnosed undulant fever, after a careful exclusion of other possibilities, was treated intramuscularly with the agent called brucellin, and in each case there was rapid and satisfactory improvement. This improvement had persisted without remission to the time of presentation of the paper.

In the summary, the unsuspected frequency of this disease was stressed, and the persistent misdiagnosis of the condition was again pointed out. It was urged that children presenting a clinical syndrome similar to that in the cases described be given the nucleoprotein skin test (Huddleson), and that in the presence of a positive intradermal test their blood be tested for phagocytic activity; it was also urged that the patients be given intramuscular injections of brucellin until their cells showed high phagocytic activity for Brucella in vitro. If an agglutination test was negative, other tests should be done (namely, the intradermal and the opsonic test) before undulant fever was definitely excluded.

Dr. I. F. Huddleson was thanked for his advice and assistance in treating the patients and in preparing the study.

DISCUSSION

QUESTION: Why were the agglutinations all negative?

DR. JOHN F. SANDER: The persistently negative agglutination test in these patients is difficult to explain. Much further work is necessary before this is

entirely clear. However, at the present time, we feel that the negative agglutination test may be disregarded in the presence of a positive skin test with negative phagocytic activity.

DR. JOHN P. PARSONS: How is brucellin prepared?

DR. JOHN F. SANDER: The preparation of brucellin (Huddleson) will be reported in the near future by Dr. Huddleson.

DR. D. MURRAY COWIE: Did I understand you to say that in most of the cases the brucellin reaction does not appear until one week after the onset of the disease?

DR. JOHN F. SANDER: At present we are unable to state definitely just how long a period elapses between the time of infection and the appearance of the positive intradermal reaction. We have not tried passive transfer into noninfected persons. The length of time a patient remains sensitized to brucellin is yet to be determined.

DR. CLEMENT A. SMITH: Can these diseases be traced to certain animals or to certain cows?

DR. JOHN F. SANDER: In the majority of cases it is extremely difficult to trace the disease to certain cows because of the multiplicity of the sources of milk in urban districts. In rural districts in which all the milk has come from the same cow or herd of cows this is frequently possible.

Dr. Beattie of Edinburgh, who is studying undulant fever with Dr. Huddleson, is with us, and I should like to have him tell you about his work with this disease in Scotland.

DR. COLIN P. BEATTIE, Edinburgh, Scotland: I have collected reports of cases of undulant fever in Scotland from the end of 1928 to September, 1932. I have found reports of only thirty-three cases. These records are, however, necessarily incomplete and do not give a true picture of the incidence of the disease. They were obtained from a few centers where blood sent to the laboratory for the routine Widal examination was tested also for the presence of agglutinins for Brucella abortus. Thus, only cases which simulated those of enteric fever were discovered, and these only in selected areas.

That the opportunity to contract undulant fever through the medium of milk is amply present in Scotland was shown by an examination of the milk supply of Edinburgh. Approximately one third of the samples of retailed raw milk I examined were found to contain Brucella abortus.

The agglutination test fails to detect a certain proportion of cases. This appears to be particularly so when the cases occur in children. On the basis of this test no cases were found in Scotland in children under 5 years of age. In England, Sir Weldon Dalrymple-Champneys recorded two cases, one in a boy of 3½ years and one in an infant of 20 months.

The new method of diagnosis with a combination of skin test and estimation of the opsonic activity presents great possibilities. Neither can be relied on alone.

Treatment by means of Dr. Huddleson's brucellin, a filtrate of a culture of the organism, has met with more consistent and rapid success than any other suggested form of treatment.

EXPERIMENTAL LIPEMIA. DR. ARTHUR CURTIS.

A person with severe diabetes who was in a state of acidosis with lipemia, lipemia retinalis and xanthomas was studied, and marked lipemia and lipemia retinalis were experimentally reproduced. The lipemia was 14.17 per cent on entrance to the hospital, and was reduced to 1.78 per cent on a diet plus insulin. A diet high in fat, carbohydrate and calories—protein, 55 Gm.; fat, 300 Gm.; carbohydrate, 270 Gm., and calories, 4,000—with insulin did not increase the lipemia. Insulin was stopped, and though a glycosuria of more than 200 Gm. daily occurred, little rise in the blood fat was noted.

By successive diets similar to the foreging one but with less carbohydrate, thereby increasing the fatty acid-globulin ratio from 0.89 to 2, an acidosis was

produced as measured by daily total excretion of acetone bodies and frequent determinations of the carbon dioxide-combining power. With the increasing acidosis, there was noted an increasing lipemia. When the carbon dioxide-combining power was 30 volumes per cent and the twenty-four hour excretion of acetone bodies in the urine 20 Gm. or more, the blood fat rose as high as 6.41 per cent.

The administration of insulin to the patient while on the same diet that produced a return of the lipemia caused the blood fat to fall to 1.08 per cent. I believe that this was due to a greater combustion of dextrose which in turn caused combustion or storage of the excess blood fat.

While the patient was on a diet high in fat with a fatty acid-globulin ratio of 2.2 and insulin, the blood fat continued to fall from 1.08 to 0.664 per cent. I feel this is further evidence that ingested fat does not cause lipemia unless it cannot be burned. Lipemia retinalis was present when the patient was first seen; it disappeared when the level of blood fat reached 3.02 per cent, and reappeared, suggestively, when the blood fat was 3.48 per cent and, positively, when the blood fat was 4.35 per cent. There seemed to be some relationship between the xanthomas and the lipemia, as yellow tumors disappeared when the blood fat was reduced to near normal levels. They did not reappear, however, when lipemia was experimentally reproduced. This may have been due to the comparatively short time the lipemia was maintained (approximately one month).

DISCUSSION

DR. JOHN P. PARSONS: This work of Dr. Curtis is extremely interesting to me. It is difficult, however, to connect this with some experimental work that I did a number of years ago. My experiments consisted of injecting acetone into animals in a dilution not sufficient to precipitate the proteins. If the dose given was not sufficiently large to kill the animal or produce a marked renal block, urine was obtained that would separate into two layers a creamy or fatty layer at the top and an ordinary layer of urine at the bottom. During this period the animal rarely had acidosis, although the acetone content in the blood was high. According to Dr. Curtis, the lipemia increases as the carbon dioxide of the blood decreases. In other words, it bears a distinct relation to the acidosis, but it must be remembered that this work is being done on persons with diabetes, and in diabetes the metabolism is fundamentally abnormal. In other words, a diabetic patient is the only type in whom acetone bears any relation to acidosis. Marked acidosis can be present in patients with a low acetone content in the blood; in fact there can be a high acetone content in the blood and the patient be in a state of alkalosis. If this work could be repeated on normal persons, it would be impossible, in my opinion, to establish a lipemia curve that would bear any relation to acidosis. It would probably, however, bear a relation to the acetone content.

DR. D. MURRAY COWIE: I should like to ask Dr. Curtis what relation the cholesterol content of the blood bears to this lipemia. Do the xanthomas so often found on the eyelids have any relation to blood fat?

DR. ARTHUR CURTIS: In reply to Dr. Parson's question, I believe that lipemia could not be produced in normal patients, because the patient has too much insulin reserve. In reply to Dr. Cowie's question, there is a relationship between the cholesterol content of the blood and the lipemia at the time of the lipemia. Fractionations of the total lipids during lipemia show definite increases in all the fundamental elements that make it up. The xanthomas found on the eyelids are not similar to the xanthoma of the diabetic patient. They are not associated with disturbed fat metabolism, but probably represent local areas of necrosis with secondary fat deposits in them which give rise to the yellow tumors commonly called xanthelasma.

REPORT ON TWO CASES OF FAMILIAL BLEEDING. DR. EVELYN WEEKS.

This article will appear in full in a later issue.

CHICAGO PEDIATRIC SOCIETY

Clinical Meeting, Jan. 17, 1933

ARCHIBALD HOYNE, M.D., *President, in the Chair*

SCARLET FEVER COMPLICATED BY LATERAL SINUS THROMBOSIS. DR. J. W. CALLAWAY.

J. B., a white male infant, aged 22 months, was admitted to the Municipal Contagious Disease Hospital on Nov. 4, 1932, because of convulsions. Examination revealed a slight nasal discharge, a red throat, cervical adenopathy, hyperactive reflexes and an unsustained ankle clonus. A diagnosis of acute pharyngitis was made.

The next day a mild punctate erythema was seen on the neck and chest, and there was a punctate rash on the soft palate. The patient's temperature was 105 F. The Dick test was negative. On November 8 a diagnosis of scarlet fever was made, and 60 cc. of scarlet fever convalescent serum was given intramuscularly. On the same day, because of a profuse seropurulent nasal discharge, a patchy membrane on the reddened throat and a musty odor, diphtheria was suspected, in spite of negative cultures, and 10,000 units of antitoxin was given intramuscularly. At this time the right tympanic membrane was bulging and both ear drums were red. The patient's face appeared puffy. There were a slight trace of blood, a trace of albumin and a few white cells in the urine.

On November 10 the face was more puffy. A paracentesis was done on the right drum, and pus was obtained. The next day the temperature was higher; a paracentesis was done on the left ear, but only blood was obtained. On November 13 there was a purulent discharge from both ears and the child had urticaria all over its body. On November 16 the count for red blood cells was 3,650,000, and for white blood cells, 34,000. Eight cubic centimeters of guaiacol and sodium iodide were given intravenously. On November 17 the child was pale and anxious. He had venous congestion and marginal infection of both eyelids. The mouth deviated to the right; the left nasolabial fold was less prominent. There was slight edema of the left mastoid region, and the left ear was more prominent than the right. Ten cubic centimeters of guaiacol and sodium iodide were given intravenously.

On November 18 Dr. Jerome Hayden saw the child; because of slight tenderness over the tip of the left mastoid and paresis of the left side of the mouth—the fundi, emissary vein, jugular vein and right mastoid being normal—lateral sinus thrombosis was suspected. A simple mastoidectomy disclosed free pus. The sinus was exposed, and free bleeding was obtained by means of a needle. There was a group of infected mastoid cells at the bend of the sinus.

On November 19 the paresis was still present. A transfusion of 180 cc. of blood was given, which was followed by an anaphylactic reaction. On December 28 the sixth blood transfusion, of 150 cc., was given. The hemoglobin was 59 per cent; there were 4,310,000 red blood cells and 20,600 white blood cells. On December 28 and 29 cultures taken from the nose and throat were positive for the diphtheria bacillus. One thousand units of antitoxin was given intramuscularly on December 29. The cultures continued to be positive until January 9, when a negative culture was obtained. On January 5 the diphtheria bacillus was cultured from the wound of the left mastoid. This organism was virulent, according to laboratory tests, but there were no clinical signs of diphtheria in the patient.

The wound of the right mastoid was closed by January 8, and the incision is now healed. The ear is still discharging moderately. The left mastoid wound is painted daily with a 2 per cent solution of gentian violet in an attempt to kill the diphtheria bacilli. The wound is healing nicely by granulation. The left ear is discharging more than the right. The various incisions made for blood transfusions and those made into the abscess have healed. With the exception of

the aural discharge, the granulating wound of the left mastoid and the facial paralysis on the left side, the child appears to be a normal healthy boy of 2 years who is getting fat.

The organism from the throat was identified by the laboratory as Streptococcus haemolyticus-scarlatinae, which produces a rather potent toxin.

DIPHTHERITIC MYOCARDITIS. DR. T. W. FALKE.

T. C., a white girl, aged 4, was admitted to the Municipal Contagion Disease Hospital on Jan. 1, 1933, with a diagnosis (made by the Health Department) of diphtheria. Prior to admission 10,000 units of antitoxin was administered. The onset of the disease was on Dec. 28, 1932.

Positive findings of the physical examination were: temperature, 100.8 F.; pulse rate, 128, and respirations, 28. There were a nasal discharge, edema of the neck and marked bilateral cervical adenitis; the mouth was open, and the tongue was coated. There was a membrane on the tonsils, soft palate and uvula, with redness and edema. The heart was enlarged slightly on the left side; the rhythm was regular, and the sounds were nearly average. The pulse was of only fair volume. An additional 20,000 units of antitoxin was administered.

On January 2, the sixth day of the disease, the temperature was 102 F. (rectal) at 4 a. m.; it gradually dropped and was 100.4 F. at 8 p. m. The pulse rate ranged between 128 and 138; respirations were between 24 and 28. The child complained of nausea and headache. A negative report for diphtheria was received for the culture taken on admission. On January 3 the temperature at 4 a. m. was 101.2 F. (rectal); it gradually became normal during the day. The patient had a poor night, sleeping little. Early in the morning she began to vomit and continued to vomit everything taken. The pulse rate fell to 80, and a beat was dropped in every four to six beats. The child was pale, fretful and very restless; the nose and lips were cyanotic.

A culture taken on January 2 was reported positive for Bacillus diphtheriae. Urinalysis showed granular and pus casts but otherwise gave negative findings.

On January 4 it was necessary to restrain the patient because of her restlessness. She slept for only short intervals. Emesis continued. She was very pale; the radial pulse was weak and irregular. The heart was slightly though definitely enlarged; the second sound was booming; the first sound was absent, except over the pulmonic area, where there was a galloping character to the rhythm. A diagnosis of diphtheritic myocarditis was made. The respirations became gasping, and soon the child apparently ceased to breathe and was pronounced dead at 9:45 a. m., on the eighth day of the disease.

Autopsy Findings.—The heart, which had stopped in systole, was pale. The endocardium had numerous red petechiae. The myocardium was pale and slightly swollen. There was an adherent long thrombus from the base of the papillary muscle in the left ventricle and in the mitral valve. A thin adherent fibrinous film was seen beneath the anterior leaf of the tricuspid valve.

The right lung was not uniformly crepitant. There were many small semisolid, shiny, dark areas, especially in the apex of the upper lobe. The process was further advanced and more widely spread in the left lung.

The kidneys were swollen, and fetal lobulations were discernible. The markings on the cut surface were obliterated; punctate hemorrhages were present in the cortex.

The liver was swollen and pale, and markings were obscured. The cut surfaces were rolled out and slate-colored.

The anatomic diagnosis was diphtheritic myocarditis, with confluent bronchopneumonia, cloudy swelling of the kidneys and fatty changes in the liver.

Summary.—A white girl, aged 4, who had never been immunized to diphtheria, contracted the disease and was ill for several days before antitoxin was administered. Cervical adenitis and marked restlessness denoted an extreme state of toxemia. Abdominal pain and vomiting indicated diphtheritic myocarditis, which was the cause of death. Autopsy confirmed this diagnosis.

EPIDEMIC MENINGITIS (MENINGOCOCCUS). DR. E. H. FELL.

R. B., a white boy, aged 11, gave a history of scarlet fever, measles, diphtheria, pertussis, varicella and parotitis. His father died of meningococcic meningitis at the Cook County Hospital after an illness of four days. The patient was admitted to the Municipal Contagious Disease Hospital on the second day of his illness, on Dec. 28, 1932. He was unruly, noisy and irrational.

Examination revealed: temperature, 102.4 F.; pulse rate, 84, and respirations, 30. The pupils gave negative findings, but there was a slight external strabismus of the left eye. There was no discharge from the nose or ears, but the left ear drum was perforated. The neck was rigid (+ + +); there was no cervical adenopathy. The mouth was open, and the tongue was coated. The throat was red, but no membrane was present. The Kernig sign was positive bilaterally. The Babinski sign was negative; there was neither clonus nor paralysis. The skin over the trunk and extremities showed numerous petechiae.

Spinal puncture revealed a cloudy fluid with a pressure of 2 +; the cell count was 14,800; the differential count showed 88 per cent polymorphonuclears and 12 per cent lymphocytes. The Ross-Jones test showed a trace; the Pandy test gave a reaction of 3 +. A smear showed intracellular and extracellular diplococci; a culture gave a growth of meningococci. Urinalysis revealed albumin 2 + and granular casts.

Treatment consisted chiefly of rest in bed and intraspinal and intravenous injections of antimeningococcic serum. Over a period of seven days 160 cc. of serum was given intraspinally, and 80 cc. was given intravenously. Spinal punctures were done on the eleventh and fourteenth days, 14 cc. and 12 cc. of serum being withdrawn on these occasions. The diet consisted of milk and orange juice and other fruit juices containing considerable additional sugar. Acetylsalicylic acid, phenobarbital and amidopyrine in small doses were employed.

On the day following admission the boy was rational and the temperature was normal. He complained of severe headache. Two or three attacks of vomiting occurred, which were described as projectile. He was restless and during the night was occasionally irrational. From that time on, his chief complaints were headache of a mild to a severe character and generalized aching. Pains in the arms began on the sixth day, and inability to extend the forearms completely was noted. The stiffness of the neck continued, as did the bilateral positive Kernig sign. There was a positive Brudzinski sign.

On the seventh day of the illness a delayed serum reaction was manifested by urticaria and a rise in temperature. On the eighth day the reaction became generalized and unpleasant. The serum sickness lasted three days.

The temperature varied from 102.4 F. on admission to 101 F. for eleven days, with elevation to 103.2 and 103.8 F. on two occasions, the latter occurring during the serum sickness. Following the last spinal puncture, on the fourteenth day, the temperature ranged from 98.8 to 99.8 F. The pulse and respirations were practically always of good quality.

The boy apparently made a complete recovery, with no residua.

SCARLET FEVER; EMPYEMA. B. O. WILSON.

CASE 1.—R. F., a boy, aged 2 years and 11 months, was admitted to the Municipal Contagious Disease Hospital on Dec. 17, 1932, on the fourth day of his illness. The essential findings were a temperature of 101.4 F., an intensely inflamed throat, a coated tongue of the strawberry type, moderate cervical adenitis and a generalized punctate erythematous rash. Scarlet fever was diagnosed.

The boy was moderately sick. Suppurative otitis media on the left side developed on the ninth day of the illness. The rash persisted until the seventh day; on the twelfth day the temperature was normal. For the following eight days convalescence appeared to be satisfactory. On Jan. 2, 1933, twenty days after the onset, the temperature suddenly rose to 103 F.; the next day it reached 105 F., and on the following day there were definite signs of a rapidly developing pleural

effusion. Physical examination of the chest had shown no signs of pneumonia. The left side of the chest was aspirated four times during the following week, on January 5, 7, 8 and 10. The pleural fluid was a thin fibrin-flaked pus. The illness terminated in death on the thirtieth day, when generalized peritonitis developed. Streptococcus haemolyticus was grown from both the pleural and the peritoneal exudates.

CASE 2.—D. W., a white girl, aged 3, was admitted to the Municipal Contagious Disease Hospital on Dec. 14, 1932, the third day after the onset of scarlet fever. She was moderately sick. Desquamation began on the ninth day of the illness. Bilateral cervical adenitis and suppurative otitis media developed. The patient was slowly convalescing when, on January 4, the twenty-fourth day of the illness, she became very sick, with a high fever and rapid grunting respirations. The next day it was apparent that empyema of the left pleural cavity was developing. There had apparently been no pneumonia.

The child is still in the hospital and is doing well under treatment by repeated aspirations.

Streptococcus haemolyticus was grown from the aspirated pus.

Comment.—These two cases of empyema caused by Streptococcus haemolyticus were presented because the condition apparently developed without preceding pneumonia and was a direct complication of scarlet fever. This combination is not frequently observed at the Municipal Contagious Disease Hospital.

DISCUSSION

DR. ARCHIBALD HOYNE: Why was the first patient admitted with a diagnosis of pharyngitis, with scarlet fever only suspected? Why was the child sent to the Municipal Contagious Disease Hospital without a definite diagnosis of infectious disease? Many patients are sent to this hospital because of suspected disorders that do not exist. This evening a child was seen who was sent in for intubation. The hospital physicians decided that the child did not have laryngeal diphtheria; they did not do an intubation. Their conclusion proved to be correct, and the child is now ready to go home.

When one sees a child at night it is difficult to decide whether the condition is laryngeal diphtheria or spasmodic croup. Consequently, when a physician sends a child with respiratory distress to the hospital, he has not made a serious mistake if he has sent the child for treatment of a disease that is not present. Several cases have been seen in which the condition was not scarlet fever, but was perhaps, pharyngitis.

At present there are several cases of epidemic meningitis in the city. Most of the patients have not been sent to the Municipal Contagious Disease Hospital, but many have been sent who presented a variety of conditions which are interesting from the standpoint of study. There have been several cases of cerebral hemorrhage, and some of pneumococcic meningitis and streptococcic meningitis; for a time it looked as though the hospital was receiving every type of meningitis except epidemic meningitis, the one variety which it is supposed to admit.

The question arises as to whether the outside physicians or the hospital physicians are correct in their diagnoses. I think that in many instances the doctor acts more wisely in sending a patient to the hospital, when the diagnosis is doubtful, than in leaving him at home with the possibility of exposure of other members of the family.

DR. S. C. PEACOCK: Are blood transfusions being used in the Municipal Contagious Disease Hospital in cases of scarlet fever?

DR. ARCHIBALD HOYNE: In some instances there have been attempts to obtain a patient who has practically recovered from the disease and to do a transfusion from that patient. The average patient with severe scarlet fever is treated with convalescent serum. Some of the patients with septic conditions receive transfusions, not necessarily from a person who has just recovered from a similar fever, but preferably so, if such a donor can be found.

Regular Meeting, Feb. 21, 1933

ARCHIBALD HOYNE, M.D., *President, presiding*

ERYTHROBLASTIC ANEMIA IN INFANCY (INAUGURAL THESIS). DR. PHILIP L. ARIES.

The disease described by Cooley and his co-workers as erythroblastic anemia has been differentiated from the indistinct group of conditions characterized by splenomegaly, leukocytosis and the presence of nucleated red blood corpuscles in the peripheral blood. Some clinicians consider this disease to be that which von Jaksch described in 1889 as pseudoleukemic anemia. Many disease processes, namely, congenital syphilis, rickets, infections and the splenic and the hemolytic anemias may produce the picture of so-called von Jaksch's anemia. Opinions also vary as to the etiology, symptomatology and prognosis of the condition. According to present knowledge, erythroblastic anemia is a clinical entity.

The sixty-three cases reported are considered to be instances of this disease. Characteristic bone changes are described in forty-nine of the reports. An additional case showing bone changes is given in this review.

All the reported cases occurred in children of the Mediterranean race. The influence of heredity has not been proved, but there is frequently a familial predisposition. The disease is congenital, the manifestations usually being evident before the second year of life. No other underlying factors, such as prematurity, nutritional disturbances, rickets, syphilis or infections, have been found to predispose to erythroblastic anemia.

The essential pathologic condition is found in the enlarged spleen and liver and in the hyperplastic bone marrow, where active hematopoiesis takes place. Peculiar structural changes are described in the bones.

Clinically, there are pallor, splenomegaly and hepatomegaly. A mongoloid facies results from hypertrophic changes in the bones of the skull. Febrile attacks, comparable to the Pel-Ebstein syndrome in Hodgkin's disease, occur. The blood has a low hemoglobin content and a low red cell count. There is a leukocytosis. Many nucleated red blood corpuscles are found in the peripheral blood. In cases in which splenectomy has been done there has been a marked permanent increase in the number of circulating erythroblasts. The red cells exhibit no tendency to assume sickle shapes. They are more resistant to dilutions of salt solution than they would be under normal conditions. The ecterus index is usually about 12. Urobilin and urobilinogen are excreted in excess. The roentgenographic examinations of the long bones, the skull and the small bones of the hands and feet reveal an increased medullary and a thinned cortical portion. Typical exaggerated trabecular markings are found. Osteoporosis is general.

The disease is chronic and progressive. The course is more acute and rapidly fatal when the condition begins during the first year of life. After months or years of invalidism, death comes as a result of an intercurrent infection or an acutely dilated heart.

The disease does not respond to known methods of treatment. The administration of liver and iron, blood transfusions, splenectomy, and roentgenotherapy to the spleen have not met with satisfactory responses.

A case was reported in which the condition was found in an Italian boy, aged 4 months. The patient was observed for fourteen months. The child died of complicating bronchopneumonia a week after this report was made. Autopsy disclosed the typical pathologic changes.

The conclusion deduced was that in erythroblastic anemia there is an inability of the organism to produce mature erythrocytes. A metabolic disturbance may be the basic abnormality. The immature cell forms are destroyed by a hemolytic process. In turn, hematopoiesis is stimulated, with resultant hyperplasia of the bone marrow and the formation of hematopoietic centers in the spleen and liver. The fact that the condition occurs in young persons and progresses slowly while growth is taking place accounts for the changes in the structure of the bones.

INCONTINENCE IN CHILDREN. DR. BERT I. BEVERLY.

This report deals with about 250 cases of incontinence (mostly nocturnal enuresis). It includes cases seen at the clinic and in private practice.

Incontinence is only one of many symptoms in every case. It is only one manifestation of a general disturbance in behavior.

Children remain infantile or return to their infancy when growing up becomes too difficult, the incontinence being one symptom of the infantilism.

The factors causing the incontinence include any innate characteristic or environmental condition which makes growing up and taking on responsibility too difficult.

The causative factors may be superficial or may include deep-seated disorders in personality.

The treatment consists in teaching the patient responsibility by psychotherapy and in adjusting environmental conditions.

It is more important to treat the underlying maladjustment than the symptom.

DISCUSSION

DR. RALPH C. HAMILL (by invitation): This subject interests me tremendously because of what we call learning as against something else that we call instinct. I think that if we could entirely understand enuresis, it might help us tremendously in understanding the physiology of excretion. Here is an act that is done supposedly in a state of unconsciousness; it starts out as a spinal reflex, but becomes a very conscious act in adult life.

If we could understand this subject better, we might become considerably enlightened on all malfunction of excretions. We might find that perhaps there is no great difference between the function of excreting urine and that of excreting feces; that there is no great difference between the function of the bladder and that of the intestines, and that both have to be learned, although at the beginning they are perfectly automatic acts.

It is interesting to think of just what goes on in the bladder. We got a fair idea of this from certain cases in which the spinal cord had been shot through; the patients were kept alive for some time and the function of their bladders studied. It was found that when about 250 cc. was allowed to flow into the bladder, there was a little resistance, and that this afterward subsided. When another 250 cc., or a total of 500 cc. was allowed to flow in, there would be another retraction, this went on until several liters of fluid were taken in, with merely this little return pressure, showing that the bladder is able to contain a large amount of liquid.

I consider that the experiment offers an answer to our question as to whether or not enuresis is dependent on the amount of liquid. It seems to me that such an explanation is ridiculous in view of this experimental proof of the bladder's ability to hold far more than these children excrete.

Urination is a conscious act. One wonders what it is in the sleeping child's mind that leads him to respond to that little momentary pressure that occurs in the bladder with the flowing in of fluid. So far as I can see, it is always an emotional force of some kind. Children are intelligent enough to know that incontinence is wrong. I have had only two of five hundred or six hundred children who would tell me why their mothers brought them to me. They had developed a sufficient sense of shame not to say out loud what was the matter with them. This fact seems to me of very great importance, for it shows that children know that incontinence is wrong. Further elaboration of that subject is ridiculous.

But there must be something going on in the child's mind that leads him to offend; because that is what it is very early in the history of these patients. There always appears to be some element of resentment in their responses. Dr. Beverly said that I think that the robbers and kidnapers and ghosts about which the children speak are their fathers. In my experience that is invariably true. The answers of the children are such that one must believe this to be true. It is the fear of the adult that leads to resentment.

It seems to me that this element of resentment is one of the things we must bear in mind if we hope to understand the subject. The various alibis that the

children give—that they play too hard, that they sleep too hard or that they have weak kidneys—are simply repetitions of what they have heard adults say.

It is interesting that so many of these children cease wetting the bed after the responsibility is placed on them. That is also a matter of technic. How is it done? One must get on some sort of friendly basis with the child in order to get him to respond. Once a 12 year old boy who was promised a thousand dollars if he quit wetting the bed for a month quit for three nights. Even to a boy of that age such a sum of money means something, but this boy held a resentment against his father that was worth more to him than the thousand dollars. One must convey to the child the idea that one is not punishing him for not accepting his responsibility. As Dr. Beverly has said, children have to have some excuse, such as bad tonsils and the like, for their incontinence. This, I believe, explains the success of many medical measures, such as tonsillectomy and circumcision. It is by assuming responsibility for themselves that they recover, and to get them to accept responsibility is the problem. Some children have such a deep resentment against adults that it is almost impossible for them to recover; they do not want to grow up.

Another important factor is the character of the dreams which these children have. I am bold enough to talk of dreams before this audience because dreams are the only record which we have of what goes on in the child's mind at such a time. In every instance in which I have been able to become friendly with a child, he has told me the same story. At 3½ years of age children begin to dream of animals that devour them. By the time they are 5 years of age, they have added to these animals human beings that also devour them; the human beings kidnap them, carry them away and eat them. However, by the time children are 7½ or 8 years of age, it is almost impossible to get them to say anything about being eaten. They have developed a fear about these dreams and will not admit it. Some children will say, "I used to think that when I was 5, but not any more." This gives us a faint suggestion of what may be going on in the child's mind; being devoured is in some way related to excretion.

Another factor should be included—that of masturbation. I am sure many of these children urinate because they handle themselves more or less in their sleep. They get erections and obvious manifestations of stimulation, and so they wet themselves in their sleep. We see those connections very clearly in the analysis of adults, and we are therefore fairly safe in conjecturing that in young children there is sexual response, which may be the element that produces the enuresis.

DR. HENRY E. IRISH: Dr. Beverly's presentation is a splendid expression of the new consciousness toward enuresis.

There is, however, so much that precedes a consideration of enuresis from a psychiatric standpoint that few of us feel sure in proceeding without knowing that all physical causes have been eliminated. I think most of us examine the urine and give the child such physical examination as we can. In addition there is the elimination of certain things, the determination of which is expensive and time-consuming, such as the determination of spina bifida and of malformations in the bladder. Some years ago I was greatly surprised to find in a child, aged 4 years, who failed to improve under the routine management a condition which was finally diagnosed as sarcoma of the prostate.

Granting that the premises are correct and that there is no physical basis for the enuresis, the discussion Dr. Beverly has given us opens up an avenue for a theory that has hitherto not been available.

In connection with the matter of evacuation of the excretory organs in the presence of fear, some light can be thrown on the subject if one considers the commonness of this reaction in the lower animals. I think that you all have tried to catch a frog in your hand, and have had evidence that he had tried to protect himself as well as he could. That means of defense is also common in cats. If you watch them trying to catch rats, you will find that the excretion of both feces and urine is a quite common defense reaction in the lower animals. The manifestation of this reflex of fear during sleep corresponds well with the idea of self-protection through excretion.

DR. ARTHUR H. PARMELEE: I hesitate to discuss, as a mere pediatrician, a question that has been so well presented from the point of view of the psychiatrist. While I agree thoroughly that in the cases reported by Dr. Beverly, and probably in the vast majority of all cases, there is a neurosis connected with enuresis—some fear or some difficulty of adjustment in the child's life, I want to call attention to the possibility that we may be laying too much stress on this subject. I cannot convince myself, in spite of my general agreement with what Dr. Beverly has said, that all cases of enuresis fall within this group.

I take issue with one point. Dr. Beverly said that enuresis never is the sole complaint, that it is always one symptom in a group of difficulties in adjustment. I cannot agree with that. It may be usually so, but I do not believe it is always so. How can we explain, for example, perfectly normal infants who continue to have enuresis from infancy, and never stop? In a family of five children that I know, of sturdy stock, in which the parents have not had time to spoil the children, and in which there has been a perfect field for developing responsibility, each child continued to have enuresis until puberty. Finally, through experience, they learned that enuresis was not proper and stopped. In addition, how shall we explain what happened during the war? In the cantonments many boys who came from the backwoods and the farms were wetting the bed. Were they problems in adjustment, or were they just boys who had grown up in the wilds who had never had this responsibility impressed on them? When they found it necessary to adjust themselves to new conditions, they stopped immediately.

While I am in thorough accord that the patients whom Dr. Beverly has seen and analyzed had problems in adjustment, for we all see cases of this sort, and although I agree that probably the majority of cases are of this sort, I can scarcely believe that all cases of enuresis can be explained on the basis of a neurosis.

I believe that there may be some constitutional basis for some cases of incontinence. When we say that all organic findings are normal, we mean that physical examination and laboratory tests gave negative results. But many constitutional disorders do not show symptoms; many disorders that really are organic in the sense that they are a part of a certain person's physical being may not give rise to objective or subjective symptoms. In some of these children there may be such a background. In the family of five that I mentioned, it is a question whether the children were subnormal, or whether there was some constitutional inferiority at the basis of the difficulty.

CHRONIC NONSPECIFIC NEPHRITIS. DR. C. A. ALDRICH and DR. HARRY H. BOYLE.

The use of the term "nonspecific" is not ideal, but it is the best term that my associate and I can think of to indicate our concept of chronic nephritis. The term implies truthfully that we do not know the cause.

The material on which the report is based consists of forty patients. The diagnostic criteria by which these patients were separated from other nephritic patients were: (1) edema, (2) arterial hypertension, (3) increase in the nonprotein nitrogenous constituents of the blood, (4) hematuria, (5) marked albuminuria, (6) cylindruria and (7) a rapidly fatal or chronic course. Every patient presented all these signs or findings at some time during the illness. If death did not occur during the first few months these manifestations fluctuated widely in severity, tending toward progressive disability. After a period of years renal insufficiency would dominate the picture, and the patient would die of true uremia, often combined with or precipitated by marked acidosis.

The onset was insidious in a large majority of the patients. Only five gave a definite history of an acute preceding febrile infection. Presenting symptoms were usually edema, albuminuria or hematuria. This type of onset contrasts sharply with that found in acute postinfectious hemorrhagic nephritis and makes us doubt the identity or chronological relationship of the two diseases.

Edema was usually found in the early stages, but was often absent during the major portion of the illness. All but one patient exhibited it at some time

or other. Many of our patients who seemed to require a salt-free regimen over a few years finally became "dry," after which salt was tolerated in large amounts. Hypertension was also commonly present early in the disease; it fluctuated to a marked degree. Acute cerebral complications did not occur as often in chronic nephritis as in the acute postinfectious type but were just as amenable to treatment in the one as in the other. Elevation of figures for the nonprotein nitrogenous constituents of the blood was often found early, but not always; the values fluctuated widely. They usually rose late in the disease. Hematuria was present to a marked degree early in the disease, but gross hematuria rarely existed for a long period. The fact that it was often absent for long periods frequently caused confusion in diagnosis, especially in differentiating the condition from nephrosis. The amount of albumin was always excessive, and our experience with this group led us to believe that albuminuria was practically constant. Casts were always found in the early stages.

Three tests of function that were easily applicable to children were used: the two hour specific gravity test, the water excretion test and the phenolsulphonphthalein test. In most instances the variation in specific gravity became less than ten points soon after the onset. The water excretion test followed the course of the edema rather closely. In most instances the output of phenolsulphonphthalein was markedly diminished rather early.

Twenty-six patients died, eleven of whom were examined post mortem. The renal lesions were absolutely diffuse, no parts of the kidneys being spared in the degenerative and sclerosing processes. The lesions were confined to the parenchyma and did not involve the blood vessels. At the time of death the patients were grossly infected in various parts of the body, whereas until a relatively short time before death little clinical evidence of microbic infection was demonstrable.

Previous to October, 1930, the treatment had consisted of a diet low in protein and measures to reduce the edema. Results had not been good. The mortality had been almost 100 per cent, and the living patients were all ill. At that time, we resolved to make a radical change. All preconceived ideas of diet were discarded, and we treated the children exactly as we should have treated any other group in as poor a nutritional state. All patients were made to observe dietary restrictions, which we hoped might compensate for any deficiency. Meat or eggs were ordered three times daily, and all available vitamins were included in the diet. Cod liver oil, yeast, orange juice, raw and cooked vegetables, and raw and cooked fruits were ordered. Salt was allowed to all who were not definitely edematous.

The results following the change were rapidly noticeable. All of the patients began to look better and were able to reenter school. Hemoglobin and weight curves rose, and marked clinical improvement was noted. Neither blood pressure nor nonprotein nitrogenous constituents of the blood rose with the change, but in many instances tended to decline. Albuminuria continued in most cases, but decreased in amount; in three instances it entirely disappeared. Red blood cells disappeared from the urine of eleven of the fourteen living patients, and casts are now a relatively rare observation.

Of ten patients put on the regimen instituted in October, 1930, only two died. The remaining eight left our care and in other institutions were given salt-free diets low in protein. We now have fourteen children under observation in the dispensary, twelve of whom have been receiving this diet for about two years. All are attending school regularly. With one exception all the children are in an excellent nutritional state, and the weight, hemoglobin and tissue turgor are good.

DISCUSSION

DR. JOSEPH BRENNEMAN: It was about eleven years ago that I first asked Dr. Aldrich to take charge of all of our nephritic patients at the Children's Memorial Hospital. I told him there were two things I was particularly interested in: First, I wanted him to show me a child who had had nephritis for six months and recovered; secondly, to show me a child who had had chronic nephritis and recovered.

His paper is an answer to the questions implied. It has been interesting, even startling, to see some of these patients with chronic nephritis who were not doing well improve markedly when they were given a general diet. I should not attribute the change to any one thing. Probably, however, the liberal amount of protein has had more to do with it than anything else. Dr. Aldrich's experiments demonstrate again that perhaps more often than is the common practice the whole child should be treated and not the symptom.

I dislike the phrase "nonspecific" as applied to chronic nephritis even more than Dr. Aldrich does. The evidence presented is interesting, but I think that in cases of this sort it is extremely difficult to exclude an initial infection and to determine definitely that the chronic nephritis has not followed an initial acute hemorrhagic nephritis. It will be interesting to follow developments along the line of this suggestion.

DR. JOSEPH K. CALVIN: Dr. Aldrich has obtained excellent results with this new therapy. His methods have already penetrated into other clinics and are being used with success. I have always agreed with him concerning most things pertaining to nephritis, but I disagree with him relative to the term "nonspecific" nephritis. At the Cook County Hospital I think we can definitely classify all our cases under the nomenclature generally accepted by the various workers in this field. That is, cases can be classified into groups of glomerulonephritis, lipoid-nephrosis, nephrosclerosis or suppurative nephritis. I believe that practically all cases can be classified thus. The condition in the cases Dr. Aldrich described, in my opinion, is simply chronic glomerulonephritis.

Dr. Aldrich bases his opinion that the syndrome which he has described is a distinct entity, differing from other forms of nephritis on the following points: 1. There is no history of an acute onset. 2. There is no preceding acute infection of the throat or of any other part of the body. 3. Acute postinfectious hemorrhagic nephritis does not become chronic. 4. Pathologically there is diffuse involvement of the kidney.

In reply to the first and second points: In routine examination of children's urine in the hospital and dispensary during epidemics of infections of the upper respiratory tract in the winter, it is not uncommon to find urine containing moderate amounts of blood, albumin and casts. These findings probably indicate cases of mild acute glomerulonephritis—cases discovered accidentally. Think of the many children on the outside who are not attended by a doctor and who may acquire a mild acute glomerulonephritis unrecognized by the parents. In these cases of mild, unrecognized, untreated glomerulonephritis the patients may recover, or they may, though probably infrequently, acquire chronic nephritis. It is possible that if these patients with cases of mild, indefinite onset could be followed up with Addis red cell counts of the urine over a period of years, it would be found that some of them are the ones who present this so-called nonspecific nephritis, which essentially is chronic glomerulonephritis for which no definite date of onset or etiology involving infection can be established. An acute infection may then develop, which causes the hidden nephritis to flare up, or renal insufficiency may develop, producing symptoms of chronic nephritis, the onset of which is in the vague past.

In reply to the third point: There is experimental evidence accumulating which indicates that glomerulonephritis may be an allergic manifestation of repeated infections of the throat with hemolytic streptococcus. It is well known that repeated mild infections with streptococci are more likely to result in allergic manifestations than a more severe infection. This may be the explanation for the fact that many patients with frank acute hemorrhagic glomerulonephritis following severe tonsillitis or other acute infection recover, although even in some of these the condition becomes chronic, while patients who have the milder, repeated infections which cause recurrent allergic renal damage acquire chronic glomerulonephritis. Another factor is that patients with severe glomerulonephritis are put to bed, kept warm and properly treated, while those with unrecognized, mild renal damage run about untreated; the condition in the latter consequently tends to become chronic.

In answer to the fourth point: The fact that all elements of the kidney are involved does not rule out glomerulonephritis. All the elements are involved in nephrosclerosis also, but any pathologist specializing in renal diseases recognizes definite changes in the kidney that characterize and distinguish one group from another; e. g., inflammatory glomerular changes in contradistinction to arteriolar sclerosis.

I feel that using the term "nonspecific nephritis" when all the other investigators working on the subject are trying to simplify the classification into the aforementioned groups is not advisable; it is confusing just at a time when we are getting out of the woods. For these reasons I feel that the term "nonspecific nephritis" should be abandoned and the cases classified under the accepted term, "chronic glomerulonephritis."

DR. JESSE R. GERSTLEY: May I ask how the diet of these children was controlled in their homes? As I understood it, most of these children were treated in the outpatient department. We all know that in outpatient departments many things are ordered that are not carried out, and it is not clear to me whether these children had a diet high in protein at home or whether they were allowed to eat what they wished. Under the latter circumstances, they might have partaken of just an ordinary diet.

DR. C. A. ALDRICH: I called this condition nonspecific nephritis in order to provoke discussion as to its etiology. I do not think that nonspecific is a good term and do not believe that it will last. I do not think that there is clinical evidence that nonspecific nephritis is from the beginning an infection. Our most brilliant example was first seen in 1922, in the dispensary; there were blood casts and pus constantly present in the urine. After two years of observation we lost track of the patient, but finally found her; she was swimming champion at one of the city parks. We lost track of her again for a time, but last summer found her again; she had just given birth to a healthy baby. The urine throughout her pregnancy was normal.

If this disease follows infections, they are so insidious that no one knows anything about them. It is strange that in following so many of these patients for so many years we did not find these infections cropping out. In only 3 per cent of our series of over two hundred patients with acute postinfectious nephritis have we failed to find a perfectly typical history of acute fulminant infection before the nephritis developed. I admit that this is a controversial point, and I have the greatest respect for Dr. Calvin's opinion. I think that we all must watch these patients to see how they turn out and to form our judgment after careful observation.

But why emphasize the glomeruli? The entire kidney is involved, and I do not think that either acute or chronic glomerular nephritis is a good term. I do not think that the rank and file of doctors when they see the patient will describe the kidney that they are going to find at necropsy. If we describe these cases accurately by clinical signs and give a clinical nomenclature, we can be sure of our ground. In the cardiac diseases we hear more and more about syphilitic myocarditis and rheumatic myocarditis and less about anatomic lesions. I think that is a decidedly advantageous method of describing diseases.

Dr. Gerstley asked how the diet was controlled. We see these patients every week or so and never fail to ask them such questions as whether they are getting meat three times a day, and whether they are getting cod liver oil. We keep the yeast on the shelf and give them that, and if they cannot get the proper food through the family funds, we ask the relief agencies to help out. We are fairly certain that our instructions are followed.

I do not wish to create the impression that we are at all dictatorial about the nomenclature, but I am glad that we used this name, because it provoked some discussion. There is great question about the etiology of the disease; careful observations will undoubtedly decide the issue.

Book Reviews

Die juvenile amaurotische Idiotie. By Thorsten Sjögren. Pp. 223. Lund: Berlingska Boktryckeriet, 1931.

This careful and thoroughgoing monograph on the juvenile form of amaurotic family idiocy merits, and will no doubt receive, a place in the standard literature on this subject. The large number of cases of this notoriously rare disease, investigated by the same observer, alone makes the work unique. The patients were mostly from state institutions for blind children in Sweden. In all, 120 examples are reported, and of these 39 were examined clinically by the author. In 18 cases the diagnosis was certified anatomically, either post mortem or from tissue obtained by puncture of the brain. The remainder of the cases were culled from the complete and reliable records kept in the institutions for many years past. The book contains excellent clinical data for all the cases.

The difficulty of making a clinical diagnosis of the Vogt-Spielmeyer form of amaurotic family idiocy is well known. According to the best opinion (Spielmeyer, Schob and others), it is considered often impossible. Sjögren thinks that now, on the basis of this material, a remarkably uniform syndrome is established which permits a diagnosis even in sporadic, nonfamilial cases and allows a differentiation from the conditions most closely simulating it, such as juvenile dementia paralytica, congenital cerebral syphilis and certain forms of diffuse sclerosis.

The leading features in this picture of progressive blindness and mental deterioration, which begins in from the fifth to the eighth years and ends in death from marasmus and intercurrent disease, after an average course of ten years, relate to findings in the fundus coupled with characteristic neurologic signs. The former comprise the findings of retinitis pigmentosa, a grayish-yellow atrophy of the papillae, pigment deposits in the retinas extending from the periphery toward the center and thinning of the vessels. Of the latter, the central position is occupied by extrapyramidal symptoms, notably stooped posture, marche à petits pas, rigid hypertonia with flexion contractures of the extremities, bradykinesia and poverty of spontaneous movement, a precipitate dysarthria with stereotypes of speech and sometimes athetoid movements. Signs of involvement of the pyramidal tract, such as the Babinski sign, are lacking or appear only terminally. Hearing is preserved.

The author considers that he has material which meets the criteria of certainty of diagnosis, purely chance incidence and uniformity of characteristics over a large series of cases, which are demanded in all investigations on the heredity of disease. Accordingly he has submitted the series to a most comprehensive genetic analysis. One hundred and fifteen cases, belonging to 59 families, were utilized, involving a consideration of 4,500 persons in collateral and ascending lines. The conclusions reached were that juvenile amaurotic family idiocy follows a recessive, monohybrid, hereditary mechanism; that thus it follows a different hereditary process than the infantile form of the disease; that the heterozygotic family lines show a clear tendency to geographic grouping within the country; that the incidence of such heterozygotes in Sweden is about 1 per cent of the general population; that the disease has been decreasing since 1917, owing to greater dispersion of the population with consequent falling off of consanguineous marriages, and that the relatives of the patients have a greater neuropathic taint with regard to epilepsy, dementia praecox and oligophrenia than the general population, but that this is proportionately no greater for any one of these conditions than for the others.

The History of Dermatology. By William Allen Pusey, Chicago. Price, $3. Pp. 223, with 28 illustrations. Springfield, Ill.: Charles C. Thomas, 1932.

This trim little volume can be perused in an evening and yet it contains an immense amount of condensed information to which one will return again and again with much profit. Pusey has a well established reputation as a pleasing writer, and his literary style enhances the sound scholarship of his matter. He has a well developed historical sense, and his introduction emphasizes that the growth of dermatology is an epitome of the evolution of modern scientific method. The first three chapters carry the reader from the earliest beginning in Egypt, thirty-five hundred years ago, to the middle of the eighteenth century. The next chapter, "Dermatology Finding Itself," treats the period from 1750 to 1825. In this age of encyclopedists it was natural that nosology was the main consideration. The attempts of Lorry, the founder of French dermatology, and Willan, the founder of English dermatology, to establish a clear definition of the terms used in the description of diseases of the skin, in order that they might found a uniform nomenclature, were productive of great good. These attempts led to careful observation, brought order out of chaos and laid a firm foundation for later advances.

The next two chapters are devoted to the threshold of modern dermatology, the period from 1800 to 1850. This was the period which followed the French Revolution. In France, particularly, the time was ripe for intellectual advance of every sort, and with the founding of the Hôpital St. Louis "there developed a group of masters who gave prestige to French dermatology including syphilography which was unchallenged until the middle of the century and which has continued until the present day." Alibert, Biett, Cazenave, Rayer, Gibert, Devergie and Bazin are household words to dermatologists everywhere. In this same period patient laboratory workers in Germany were preparing the way for the modern period. Von Bärensprung described the essential lesion of herpes zoster in the spinal ganglion. Schönlein discovered the fungus origin of favus and founded microparasitology.

The remaining three chapters summarize in brilliant fashion the triumphs of modern dermatology. Ferdinand Hebra, a pupil of Rokitansky and Skoda, was a product of the new era of clinical investigation and of a great institution of clinical research, the Allgemeines Krankenhaus, where laboratory methods were intensively used in the study of disease, a triumph of the German method. In Pusey's pages he lives again with his pupil Moritz Kaposi. Then follow short but incisive sketches of the more modern masters, Unna, Neisser, Boeck, Duhring, Hutchison, Brocq and many others. Pusey has expended great effort in collecting reproductions of the available portraits of the masters of dermatology, giving the reader added interest.

The final section, "An Historical Index of Dermatology," is a unique contribution. The diseases are arranged in alphabetical order and each is followed by the name of the author who first described the entity, with the date. This is followed by one or two references to authoritative papers in the modern literature. This little index is invaluable as a quick and ready reference. It gives in condensed form the result of a great amount of historical research.

As the first history of dermatology in English, Pusey's work supplies a definite need, and its inspiring pages should prove a stimulus to the younger generation to which it is dedicated.

Criteria for the Classification and Diagnosis of Heart Disease. By the Criteria Committee of the Heart Committee of the New York Tuberculosis and Heart Association, Inc. Third edition. Price, $1. Pp. 131. New York: Tuberculosis and Health Association, 1932.

The committee has enlarged the list of diagnostic titles and rearranged their order with grouping under anatomic headings referable to the part of the cardiovascular system affected. This amplification makes it possible to find suitable terms for all types of cardiac disease. Another advantage is the ready coordination

with the cardiac section of the Standard Classified Nomenclature of Disease prepared by the National Conference on Nomenclature of Disease published in January, 1933.

The nomenclature is divided into:

(*A*) Etiologic diagnosis, such as anemia, arteriosclerosis, bacterial infection and rheumatic fever.

(*B*) Anatomic diagnosis, such as aorta and pulmonary artery; coronary arteries; endocardium, myocardium and valves and pericardium.

(*C*) Physiologic diagnosis, such as anginal syndrome, bundle branch block and premature contractions.

(*D*) Functional capacity.

(*E*) Possible heart disease.

(*F*) Potential heart disease.

The criteria for diagnosis of the various diseases are grouped in detail under headings of etiologic, anatomic, physiologic and functional capacity. The patients are classified under the following grouping:

Class I: Patients with organic lesions who manifest ordinary physical activity and no discomfort.

Class II: Patients with organic lesions who are unable to carry on ordinary physical activity without discomfort, including (*a*) those whose activity is slightly limited and (*b*) those whose activity is greatly limited.

Class III: Patients with organic cardiac disease and with symptoms or signs of cardiac insufficiency at rest who are unable to carry on any physical activity without discomfort.

Class E: Patients who have abnormal signs or symptoms referable to the heart, but in whom the diagnosis of cardiac disease is uncertain. This condition should be diagnosed as "possible heart disease, class E."

Class F: Patients without cardiac disease whom it is advisable to follow up because of the presence or history of an etiologic factor which might cause cardiac disease. This condition should be diagnosed as "potential heart disease, class F."

The appendix is a guide to roentgenologic diagnosis in cardiac disease, with a short discussion of the various lesions. It contains diagrams elucidating the various silhouettes of the roentgenogram and fluoroscope. The criteria for interpretation of electrocardiograms are amplified, with specimen tracings illustrating the various deviations of rhythm and voltage.

Die Tuberkulose des Kindesalters. By F. Hamburger and K. Dietl. Third edition. Price, 16 marks. Pp. 300. Vienna: Franz Deuticke, 1932.

The first edition of the monograph on tuberculosis in childhood appeared in 1909. This edition is subdivided into a theoretical and a practical part. The theoretical phase of tuberculosis is based largely on the senior author's laboratory observations on lower animals, and the practical part is devoted to the clinical phases of tuberculosis in childhood.

As in any other branch of medicine, views and hypotheses in regard to tuberculosis are constantly undergoing considerable metamorphosis, so that what appeared to be valid in 1909 may be entirely invalidated by 1932. The views expressed in this volume in regard to the theoretical phases of tuberculosis differ but little from those uttered by the senior author in 1911, and, as stated, are based largely on his own experimentations on animals between 1909 and 1911. Thus the all important question as to the relation of allergy to immunity, which prompted considerable discussion and experimentation in this country, is almost entirely neglected, while the descriptions of individual animal experiments could have been abbreviated and made more precise. The views of the most prolific workers in this field in America, notably Krause, Opie and Rich, are not even mentioned, let alone discussed.

The authors' views on the prognostic value of the reaction to tuberculin will also be questioned by the pediatrician and the student of tuberculosis.

The monograph lacks certain attributes which would make it suitable to the pediatrician or to the laboratory investigator in tuberculosis. It does not contain a single x-ray illustration, and hence the clinician will find the book valueless if he is seeking for the roentgenographic appearance of the lungs, say, in epituberculosis, or even in the more common types of tuberculous infections. The experimental worker in this field is probably acquainted with more recent views than can be found in this volume.

Pediatric Nursing: The Nurses' Text Book Series. By Abraham Levinson, B.S., M.D. Second edition. Price, $2.75. Pp. 282, with 28 illustrations. Philadelphia: Lea & Febiger, 1933.

This volume is written in an interesting manner and should be of value to every nurse. The latest nursing procedures used in pediatrics are explained. The author discusses concisely and clearly each disease in regard to its etiology, symptoms and treatment, including cases in which special nursing is necessary. Complete and valuable instruction is given the nurse in caring for patients in emergency cases before and after the physician's arrival. The chapters dealing with the psychology of caring for children and the nurse's attitude toward parents are well written. On the whole, the book is a most practical text for both student and graduate nurses.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.
Secretary: Dr. Leonard K. Findlay, 61 Harley St., London, W. 1.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. Leonard G. Parsons, 58, Calthorpe Road, Birmingham, England.
Secretary: Dr. W. G. Wyllie, 33, Wimpole St., W. 1, London.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Frederic W. Schlutz, Bobs Roberts Hospital, University of Chicago, Chicago.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: Milwaukee. Time: June 12-16, 1933.

American Academy of Pediatrics

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Section on Children's Hospitals

President: Dr. Thomas B. Cooley, 7815 E. Jefferson Ave., Detroit.
Secretary: Miss Bena M. Henderson, 721 N. 17th St., Milwaukee.

American Pediatric Society

President: Dr. Charles A. Fife, 2104 Spruce St., Philadelphia.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Asheville, N. C. Time: May, 1934.

Canadian Society for the Study of Diseases of Children

President: Dr. Frederick F. Tisdall, 170 St. George St., Toronto, Ontario.
Secretary-Treasurer: Dr. T. G. H. Drake, 67 College St., Toronto, Ontario.

Society of Pediatric Research

President: Dr. Rustin McIntosh, College of Physicians and Surgeons, Columbia University, New York.
Secretary-Treasurer: Dr. Charles F. McKhann, Harvard Medical School, Boston.
Place: Atlantic City, N. J. Time: May, 1934.

SECTIONAL

Central States Pediatric Society

President: Dr. Julius H. Hess, 104 S. Michigan Ave., Chicago.
Secretary: Dr. A. H. Parmelee, 715 Lake St., Oak Park, Ill.
Place: Chicago. Time: Sept. 22-23, 1933.

North Pacific Pediatric Society

President: Dr. Herbert E. Coe, 509 Olive St., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Hugh L. Dwyer, 406, W. 34th St., Kansas City, Mo.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Place: Richmond, Va. Time: November, 1933.

STATE

Alabama Pediatric Society

President: Dr. C. E. R. Parker, 401 S. Court St., Montgomery.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

Georgia Pediatric Society

President: Dr. Joseph Yampolsky, 311 Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Atlanta. Time: October, 1933. Augusta. Time: May, 1934.

Louisiana State Pediatric Society

President: Dr. Cecil O. Lorio, 245, 3d St., Baton Rouge.
Secretary-Treasurer: Dr. Maud Loeber, 3503 Prytania St., New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Adolph G. De Sanctis, 12 E. 11th St., New York.
Secretary: Dr. George M. Retan, 459 James St., Syracuse.

Nebraska Pediatric Society

President: Dr. W. O. Colburn, 724 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. C. G. Weigand, 1614 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. J. Buren Sidbury, 15 N. 5th St., Wilmington.
Secretary: Dr. E. K. McLean, 121 W. 7th St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. Clark H. Hall, 117 N. Broadway, Oklahoma City.
Secretary: Dr. M. J. Searle, 108 W. 6th St., Tulsa.

South Carolina Pediatric Society

President: Dr. J. I. Waring, 77 Rutledge Ave., Charleston.
Secretary-Treasurer: Dr. Julian P. Price, Medical Bldg., Florence.

Texas Pediatric Society

President: Dr. Sidney R. Kaliski, Moore Bldg., San Antonio.
Secretary-Treasurer: Dr. Frank M. Martin, 321 Medical Arts Bldg., San Antonio.

Virginia Pediatric Society

President: Dr. J. B. Stone, 2042 Park Ave., Richmond.
Secretary-Treasurer: Dr. Thomas D. Jones, Medical Arts Bldg., Second and Franklin Streets, Richmond.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. George M. Lyon, 955, 4th Ave., Huntington.
Secretary: Dr. M. F. Petersen, 1013 Quarrier St., Charleston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. C. W. Burhans, 14805 Detroit Ave., Lakewood, Ohio.
Secretary: Dr. J. A. Garvin, 2009 Adelbert Road, Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

Bronx Pediatric Society

President: Dr. Edward L. Benjamin, 2021 Grand Concourse, New York.
Secretary: Dr. Harry M. Schapiro, 1882 Grand Concourse.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Every Second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Archibald L. Hoyne, 25 E. Washington St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Bernard Bernbaum, 5057 Woodward Ave., Detroit.
Secretary: Dr. Sarah S. Schooten, 5057 Woodward Ave., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

International Pediatric Society

President: Dr. Barnet E. Bonar, 9 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Memphis Pediatric Society

President: Dr. R. B. McCormick, 1074 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. D. Mims, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. Karl E. Kassowitz, 709 N. 11th St., Milwaukee.
Secretary: Dr. John H. Reynolds, 747 N. 27th St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Thomas A. Foster, 131 State St., Portland, Maine.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Martha Wollstein, Babies' Hospital of City of New York, New York.
Secretary: Dr. Harry Bakwin, 132 E. 71st St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. Loyd Hardgrave, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Roland P. Seitz, 490 Post St., San Francisco.

Northwestern Pediatric Society

President: Dr. Irving McQuarrie, Dept. Pediatrics, University of Minnesota, Minneapolis.
Secretary: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.

Philadelphia Pediatric Society

President: Dr. Joseph Stokes, 159 W. Coulter St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. Henry C. Flood, 119 S. Highland Ave., Pittsburgh.
Secretary: Dr. E. R. McCluskey, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. F. Waring Lewis, Professional Bldg., Richmond, Va.
Secretary-Treasurer: Dr. A. S. Hurt, Jr., 2618 Grove Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. S. W. Clausen, Strong Memorial Hospital, Rochester, N. Y.
Secretary: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. J. A. Schoonover, Republic Bldg., Denver.
Secretary: Dr. Arthur L. Esserman, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7 p. m.

St. Louis Pediatric Society

President: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Albert S. McCown, 509 Olive St., Seattle.
Secretary: Dr. Frank H. Douglass, Medical-Dental Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. James E. Harvey, 60 S. Lake Ave., Pasadena, Calif.
Secretary: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Gustave F. Weinfeld, Moraine Hotel, Highland Park, Ill.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: November, 1933.

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